Bioinformatics analysis of potential key genes and mechanisms in type 2 diabetes mellitus

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

Type 2 diabetes mellitus (T2DM) is etiologically related to metabolic disorder. The aim of our study was to screen out candidate genes of T2DM and to elucidate the underlying molecular mechanisms by bioinformatics methods. Expression profiling by high throughput sequencing data of GSE154126 was downloaded from Gene Expression Omnibus (GEO) database. The differentially expressed genes (DEGs) between T2DM and normal control were identified. And then, functional enrichment analyses of gene ontology (GO) and REACTOME pathway analysis was performed. Protein–protein interaction (PPI) network and module analyses were performed based on the DEGs. Additionally, potential miRNAs of hub genes were predicted by miRNet database . Transcription factors (TFs) of hub genes were detected by NetworkAnalyst database. Further, validations were performed by receiver operating characteristic curve (ROC) analysis and real-time polymerase chain reaction (RT-PCR). In total, 925 DEGs were identified in T2DM, including 447 up regulated genes and 478 down-regulated genes. Functional enrichment analysis results showed that up regulated DEGs were significantly enriched in defense response, neutrophil degranulation, cell adhesion and extracellular matrix organization. The top 10 hub genes, JUN, VCAM1, RELA, U2AF2, ADRB2, FN1, CDK1, TK1, A2M and ACTA2 were identified from the PPI network, modules, miRNA-hub gene regulatory network and TF-hub gene regulatory network. Furthermore, ROC analysis and RT-PCR revealed that JUN, VCAM1, RELA, U2AF2, ADRB2, FN1, CDK1, TK1, A2M and ACTA2 might serve as biomarkers in T2DM. Bioinformatics analysis is a useful tool to explore the molecular mechanism and pathogenesis of T2DM. The identified hub genes may participate in the onset and advancement of T2DM and serve as therapeutic targets.

Keywords: biomarker; differentially expressed genes; type 2 diabetes mellitus; bioinformatics; protein–protein interaction network

Introduction

Type 2 diabetes mellitus (T2DM) is the most common chronic metabolic disorder in adults and its affects more than 90% people worldwide [1]. The incidence rate of T2DM is high, which vigorously affects the patient's health. T2DM can affect the brain [2], kidney [3], eyes [4] and heart [5]. Numerous risk factors might affect T2DM progression, including genetic [6], environmental [7] metabolic [8] risk factors, obesity [9] and hypertension [10]; however, how these factors affect the progression of T2DM requires further investigation and no effective treatment has been advanced for the relief of T2DM. In addition, molecular biology investigation have identified numerous biomarkers and signaling pathways that contribute to T2DM, including the OCT1 [11], TNF-α [12], TCF7L2 [13], KCNJ11 [14], SDF-1β [14], EDNRB [15], NOS3 [15], PI3K/AKT pathway [16], IL-6 signalling pathways [17], Wnt signaling pathway [18], insulin signaling [19] and NF-κB signaling pathway [20]. Further investigation into the molecular events linked with T2DM progression is required.

With the advancement of molecular biological and pathological techniques, a range of markers are considered powerful tools for searching diagnostic and predictive biomarkers, especially in the therapies targeting T2DM. Expression profiling by high throughput sequencing, efficient and large-scale techniques for gaining genetic data, have been widely performed to collect and to study Expression profiling by high throughput sequencing data in T2DM. These high throughput sequencing studies develop a novel approach for identifying T2DM related genes and implement encouraging expectation for molecular prediction and therapeutic targets [21].

In the current investigation, the expression profiling by high throughput sequencing data of GSE154126 [22] was downloaded from Gene Expression Omnibus (GEO, http://www.ncbi.nlm.nih.gov/geo/) [23] to screen the differentially expressed genes (DEGs) between T2DM and normal control. Next, the DEGs were analyzed using a bioinformatics approach. To identify the enriched biological functions and pathways of DEGs, the Gene Ontology (GO) and REACTOME pathway enrichment analysis of DEGs were performed. Subsequently, functional enrichment, protein-protein interaction (PPI) networks construction, module analyses and miRNA-hub regulatory gene network

construction and TF-hub regulatory gene network construction were performed to determine the significant pathogenic genes and their key pathways involved in the mechanism of occurrence and progression of T2DM. Hub genes were validated using the receiver operating characteristic curve (ROC) analysis and RT-PCR. These results may provide information for subsequent experimental studies of T2DM, and contribute to the understanding of the molecular mechanisms underlying the advancement of T2DM.

Material and Methods

RNA sequencing data

The expression profiling by high throughput sequencing of GSE124742 was downloaded from the GEO database. The data were produced based on the GPL11154 platform Illumina HiSeq 2000 (Homo sapiens). The GSE154126 dataset contained 1276 samples, including 508 samples of T2DM samples and 768 normal control samples.

Identification of DEGs

The limma package [24] in R Bioconductor was used to identify DEGs between T2DM samples and normal control samples. The P-values of DEGs were calculated using a t-test in R with the limma package. P value <0.05, $|\log FC| > 0.63$ for up regulated genes and $|\log FC| < -1.99$ for down regulated genes were set as the cutoff criterion for statistically significant DEGs. In this investigation, ggplot2 and the gplots in R package were used to plot the volcano diagrams and heat map of the DEGs, respectively.

Gene Ontology (GO) and REACTOME pathway enrichment analysis

Gene Ontology (GO) (http://geneontology.org/) [25] and REACTOME (https://reactome.org/) [26] pathway enrichment analyses of T2DM DEGs were performed using ToppGene (ToppFun) (https://toppgene.cchmc.org/enrichment.jsp) [27]. GO terms of biological processes (BP), cellular components (CC), and molecular functions (MF) linked with a p-value <0.05 were considered to be significantly enriched.

PPI network construction and module analysis

The online IntAct interactome (https://www.ebi.ac.uk/intact/) [28] database was used to identify potential interaction among the common DEGs, and a confidence score of ≥0.4 was set as the threshold. Cytoscape software, version 3.8.2 (www.cytoscape.org) [29] was used to visualize the PPI network of common DEGs. The Network Analyzer plug-in was used to calculate node degree [30], betweenness centrality [31], stress centrality [32] and closeness centrality [33], that were to filter hub genes of PPI. The PEWCC1 (http://apps.cytoscape.org/apps/PEWCC1) [34] was used to search modules of the PPI network and the default parameters (Degree cutoff ≥10, node score cutoff ≥0.4, K-core ≥4, and max depth=100.) were set in the functional interface of Cytoscape software.

MiRNA-hub gene regulatory network construction

miRNet database (https://www.mirnet.ca/) [35] for miRNA-hub gene regulations, through which regulatory associations between hub genes and miRNAs can be identified. This study inputted the overlapped hub genes into the database to examine the regulatory association pairs between miRNAs and hub genes. Based on the data this study obtained, miRNA-hub gene regulatory network was constructed and visualized by Cytoscape 3.8.2 software to show the overlapped miRNAs and hub genes. Therefore, these miRNAs and hub genes might play a potential role in the pathogenesis and treatment of T2DM.

TF-hub gene regulatory network construction

NetworkAnalyst database (https://www.networkanalyst.ca/) [36] for TF-hub gene regulations, through which regulatory associations between hub genes and TFs can be identified. This study inputted the overlapped hub genes into the database to examine the regulatory association pairs between TFs and hub genes. Based on the data this study obtained, TF -hub gene regulatory network was constructed and visualized by Cytoscape 3.8.2 software to show the overlapped TFs and hub genes. Therefore, these TFs and hub genes might play a potential role in the pathogenesis and treatment of T2DM.

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

Genes in the PPI network identified by Network Analyzer plug-in were selected as candidate hub genes. To evaluate the role of candidate genes in the diagnosis of T2DM, receiver operating characteristic (ROC) curve analysis was organize in RStudio with pROC package [37]. The genes with area under curve (AUC) >0.8 was considered as hub genes of T2DM.

Detection of the mRNA expression of the hub genes by RT-PCR

Total RNA was isolated from RIN5F cells, insulin secreting rat pancreatic β cell line treated with streptozotocin for T2DM and RIN5F cells, insulin secreting rat pancreatic β cell line for normal using TRI Reagent (Sigma, USA) according to the instructions. RNA samples were reverse transcribed into cDNA by FastQuant RT kit (with gDNase; Tiangen Biotech Co., Ltd.). RT-PCR analysis was performed QuantStudio 7 Flex real-time PCR system (Thermo Fisher Scientific, Waltham, MA, USA). The set of primers used in the investigation is listed in Table 1.The experiment was repeated in triplicate. PCR profiles used in this investigation were: denaturing for 10 min at 95°C, annealing for 15 sec at 95°C, and extension for 10 sec at 72°C. PCR was carried out for 30 cycles. The relative value of the hub gene was normalized to those of β-actin through the $2^{-\Delta\Delta Ct}$ calculation [38].

Results

Identification of DEGs

Standardization of the expression profiling by high throughput sequencing results from GSE124742, DEGs were identified. A total of 925 differentially expressed genes including 447 up regulated genes and 478 down regulated genes were detected and are listed in Table 2. The results were validated with a volcano plot of all up regulated genes and down regulated genes (Fig.1). Fig. 2 shows the DEG expression heat map.

Gene Ontology (GO) and REACTOME pathway enrichment analysis

GO enrichment analysis showed that the DEGs were mainly involved in defense response, secretion, secretory vesicle, golgi apparatus, identical protein binding, transmembrane transporter activity, cell adhesion, localization of cell, extracellular matrix, intrinsic component of plasma membrane, structural molecule activity and signaling receptor binding, and are listed in Table 3. REACTOME pathway

enrichment analysis revealed that the DEGs were mainly enriched in the neutrophil degranulation, innate immune system, extracellular matrix organization and diseases of glycosylation, and are listed in Table 4.

PPI network construction and module analysis

The PPI network of DEGs was constructed with 7195 nodes and 16541 edges (Fig.3). The node degree, betweenness centrality, stress centrality and closeness centrality methods were performed to calculate the top ranking hub genes. The results revealed 10 genes identified as hub genes, including JUN, VCAM1, RELA, U2AF2, ADRB2, FN1, CDK1, TK1, A2M and ACTA2, and are listed Table 5. PEWCC1 was used to identify the two significant cluster modules in the PPI network and the top modules were selected (Fig.4A and Fig.4B). Gene Ontology (GO) and REACTOME pathway enrichment analysis revealed that the module 1 (48 nodes and 104 edges) and module 2 (30 nodes and 92 edges) were mainly enriched in cytokine signaling in immune system, identical protein binding, neutrophil degranulation, golgi apparatus, innate immune system, extracellular matrix organization, axon guidance, cell adhesion, platelet activation, signaling and aggregation, diseases of glycosylation, hemostasis, extracellular matrix, localization of cell and structural molecule activity.

MiRNA-hub gene regulatory network construction

The miRNA-hub gene regulatory network was shown in Fig. 5, consisting of 2807 nodes and 21728 interactions. MiRNAs includes hsa-mir-1255b-5p, hsa-mir-499a-5p, hsa-mir-200a-3p, hsa-mir-449c-5p, hsa-mir-520a-5p, hsa-mir-410-3p, hsa-mir-3941, hsa-mir-181d-3p, hsa-mir-181c-5p and hsa-mir-708-5p were with the highest connectivity target genes, targeting 10 hub genes (up regulated: MRPL12, RAB5C, VCAM1, HIF1A and CLU; down regulated: CDK1, CHEK1, TK1, KIT and TOP2A) and are listed in Table 6. **TF-hub gene regulatory network construction**

The TF-hub gene regulatory network was shown in Fig. 6, consisting of 625 nodes and 10244 interactions. TFs includes VDR, BACH1, TFCP2L1, HOXC9, GATA2, TBX3, ATF3, GATA4, PAX6 and FOXP1 were with the highest connectivity target genes, targeting 10 hub genes (up regulated: JUN, POLR2A, HIF1A,

MRPL12 and U2AF2; down regulated: RPTOR, FN1, ANLN, MME and HEY1) and are listed in Table 6.

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

Validate the expression of these 10 genes in T2DM and performed ROC analysis in RStudio with pROC package. The analysis results were available in Fig.7. Ten genes (JUN, VCAM1, RELA, U2AF2, ADRB2, FN1, CDK1, TK1, A2M and ACTA2) with AUC more than 0.90 were considered as hub genes, indicating that they have the capability to diagnose T2DM patients with excellent specificity and sensitivity.

Detection of the mRNA expression of the hub genes by RT-PCR

To further verify the expression level of hub genes in T2DM **(**RIN5F cell line treated with streptozotocin) and normal **(**RIN5F cell line), RT-PCR was performed to calculate the mRNA levels of the ten hub genes identified in the present study (JUN, VCAM1, RELA, U2AF2, ADRB2, FN1, CDK1, TK1, A2M and ACTA2) in T2DM. As illustrated in Fig. 8, the expression of JUN, VCAM1, RELA, U2AF2 and ADRB2 were significantly upregulated in T2DM compared with normal, while FN1, CDK1, TK1, A2M and ACTA2 were significantly upregulated in T2DM compared with normal. The current RT-PCR results were in line with the previous bioinformatics analysis, suggesting that these hub genes might be associate to the molecular mechanism underlying T2DM.

Discussion

T2DM is a complex metabolic disorder characterized by defective glucose uptake in muscle and fat, varied glucose-induced insulin secretion, and heightened hepatic glucose production. It is largely ascribed to insulin resistance and leads in a heavy health and economic burden. Therefore, it is important to study the molecular mechanism of T2DM. In this investigation, we tried to identify the important genes related to T2DM by comparing the differences in expression profiling by high throughput sequencing between the T2DM and normal controls. A total of 925 DEGs (447 up regulated genes and 478 down regulated genes) were screened between T2DM and control samples. Emmens et al [39] found that PENK

(proenkephalin) expression was up regulated in cardiovascular diseases, but this gene might be responsible for progression of T2DM. Recent studies have proposed that the SAA1 [40], SUCNR1 [41], CRP (C-reactive protein) [42], APCS (amyloid P component, serum) [43], PCK1 [44], IGF2BP3 [45], POSTN (periostin) [46] and COL6A3 [47] are associated with progression of T2DM. CARTPT (CART prepropeptide) [48], SEMA3C [49] and TDO2 [50] were proved to participate in the development of obesity, but these genes might be linked with progression of T2DM. SOX11 is associated with progression of neurological disorders [51], but this gene might be liable for advancement of T2DM.

The functional enrichment analysis indicated that the DEGs were primarily involved in the defense response, secretory vesicle, identical protein binding, cell adhesion, extracellular matrix, structural molecule activity, neutrophil degranulation and extracellular matrix organization. Neutrophil degranulation [52], innate immune system [53], platelet degranulation [54], extracellular matrix organization [55], diseases of glycosylation [56], platelet activation, signaling and aggregation [57], hemostasis [58], secretion [59], secretory vesicle [60], transmembrane transporter activity [61], cell adhesion [62], localization of cell [63], extracellular matrix [55], intrinsic component of plasma membrane [64], structural molecule activity [65], signaling receptor binding [66], have been highly noted in T2DM. Reports indicate that HIF1A [67], HLA-DRB1 [68], CHI3L1 [69], ADORA2A [70], ADRB2 [71], CLU (clusterin) [72], AGT (angiotensinogen) [73], VCAM1 [74], PPARA (peroxisome proliferator activated receptor alpha) [75], APOL1 [76], ZFP36 [77], PPM1B [78], SOCS1 [79], SNCA (synuclein alpha) [80], CTSS (cathepsin S) [81], IL6R [82], CFB (complement factor B) [83], DEFB1 [84], VNN1 [85], RAB27A [86], DPP4 [87], RARRES2 [88], CASP1 [89], LCN2 [90], REG3A [91], CD74 [92], PCSK2 [93], CHGB (chromogranin B) [94], TTR (transthyretin) [95], LRG1 [96], ALB (albumin) [97], DPP7 [98], APOH (apolipoprotein H) [99], CTSD (cathepsin D) [100], GCG (glucagon) [101], KCNQ1 [102], NR4A1 [103], PLIN5 [104], ALDH2 [105], ANG (angiogenin) [106], CLDN7 [107], PRLR (prolactin receptor) [108], SOD2 [109], MLXIPL (MLX interacting protein like) [110], CTSD (cathepsin D) [111], PECAM1 [112], ADA (adenosine deaminase) [113], MFGE8 [114], COL1A1 [115], COL3A1 [116], NID2 [117], ARG1 [118], CD93 [119], IGF2 [120], IL18 [121], LAMA1 [122], HPSE (heparanase) [123], BMP4 [124], CXCR4 [125], KDR (kinase insert

domain receptor) [126], ESAM (endothelial cell adhesion molecule) [127], THBS1 [128], CD34 [129], SERPINE1 [130], WNT5B [131], MGP (matrix Gla protein) [132], MMP3 [133], MMP9 [134], MMP11 [135], IL16 [136], TNFRSF11B [137], TIMP3 [138] and CAPN3 [139] were found in T2DM. HLA-A [140], HLA-B [141], HLA-C [142], HLA-DPB1 [143], HLA-E [144], ERBB3 [145], MFAP4 [146] and JAK3 [147] have been reported significantly expressed in type 1 diabetes mellitus, but these genes might be involved in T2DM progression. HLA-DRA [148], SERPINA1 [149], ABHD12 [150], IMPA2 [151], ARSA (arylsulfatase A) [152], LRFN5 [153], PLXNA4 [154], CHL1 [155], ITPKB (inositol-trisphosphate 3-kinase B) [156], PTN (pleiotrophin) [157], LAMA2 [158], CDH6 [159] and A2M [160] have been shown to have an important role in neurological disorders, but these genes might be associated with progression of T2DM. HLA-F [161], HLA-H [162], FGA (fibrinogen alpha chain) [163], HSPA1B [164], MRC1 [165], DAB2IP [166], KCNJ8 [167], KLKB1 [168], CXCL2 [169], SERPINE2 [170], ADH1C [171], AMBP (alpha-1-microglobulin/bikunin precursor) [172], NR4A2 [173], TYMP (thymidine phosphorylase) [174], TFRC (transferrin receptor) [175], PLAU (plasminogen activator, urokinase) [176], COL6A2 [177], COL15A1 [178], ABI3BP [179], NEXN (nexilin F-actin binding protein) [180], S1PR1 [181], THY1 [182], COL4A1 [183], COL5A2 [184], ADAMTS2 [185], ECM1 [186] and LTBP2 [187] have been found to be differentially expressed in cardiovascular diseases, but these genes might be linked with progression of T2DM. CCL20 [188], CRH (corticotropin releasing hormone) [189], SPP1 [190], LDLR (low density lipoprotein receptor) [191], RORA (RAR related orphan receptor A) [192], LYZ (lysozyme) [193], PTPRN2 [194], DAPK2 [195], OIP5 [196], PON3 [197], NR4A3 [198], VCAN (versican) [199], CNTNAP2 [200], IL1RAP [201], GLI2 [202], CDH13 [203], AEBP1 [204], BGN (biglycan) [205], LOX (lysyl oxidase) [206], IL1RL1 [207] and LUM (lumican) [208] were found to be involved in advancement of obesity, but these genes might be key for development of T2DM. C4BPA [209], KYNU (kynureninase) [210], ORM1 [211], ARSA (arylsulfatase A) [212], CYB5R3 [213], MAT1A [214], SDC4 [215], ASL (argininosuccinate lyase) [216], SLC4A4 [217], EPHB6 [218], SPARCL1 [219], THBS2 [220], EFNB2 [221] and CD248 [222] were revealed to be associated with hypertension, but these genes might be involved in progression of T2DM. GSDMD (gasdermin D) [223],

UNC5B [224] and PDGFB (platelet derived growth factor subunit B) [225] have been reported significantly expressed in diabetic nephropathy.

A PPI network and modules was constructed and analyzed with DEGs, and then hub genes were identified. Gregg et al [226] revealed that CDK1 involvement in of obesity, but this gene might be associated with advancement of T2DM. ACTA2 was revealed to be associated with development of T2DM [227]. JUN (jun proto-oncogene, AP-1 transcription factor subunit), RELA (RELA proto-oncogene, NF-kB subunit), U2AF2, TK1, RAB5C, OCRL (OCRL inositol polyphosphate-5-phosphatase), COL5A1, FN1, SPARC (secreted protein acidic and cysteine rich), TGFBI (transforming growth factor beta induced) and COL1A2 might be the novel biomarkers for the advancement of T2DM.

In this investigation, miRNA-hub gene regulatory network and TF-hub gene regulatory network were constructed and analyzed. Demirsoy et al [228], Hourigan et al [229], Safar et al [230], Zmuda et al [231], Boese et al [232] and Suhara et al [233] found that hsa-mir-200a-3p, hsa-mir-181c-5p, VDR (vitamin D receptor), ATF3, PAX6 and RPTOR (regulatory associated protein of MTOR complex 1) were participating in the occurrence and development of T2DM. Cabiati et al [234] and Patankar et al [235] proved that hsa-mir-410-3p and GATA4 mediate the development of obesity, but these genes might be associated with development of T2DM. Hsa-mir-3941 [236], BACH1 [237], GATA2 [238], FOXP1 [239] and HEY1 [240] were found to be involved in the process of cardiovascular diseases, but these genes might be associated with development of T2DM. Hsa-mir-708-5p was revealed to be correlated with disease outcome in patients with neurological disorders [241], but this gene might be linked with development of T2DM. A previous study found that MRPL12 [242] and MME (membrane metalloendopeptidase) [243] expression could enhance the diabetic nephropathy. A previous study showed that CHEK1 gene is involved in the hypertension [244], but this gene might be associated in development of T2DM. Hsa-mir-1255b-5p, hsa-mir-499a-5p, hsa-mir-449c-5p, hsa-mir-520a-5p, hsa-mir-181d-3p, TFCP2L1, HOXC9, TBX3, KIT (KIT proto-oncogene, receptor tyrosine kinase), TOP2A, POLR2A and ANLN (anillin actin binding protein) might be the novel biomarkers for the advancement of T2DM.

In conclusion, the current investigation exhibits the global profile of DEGs and relative signaling pathways that might participate in the initiation and advancement of T2DM. In the pathogenesis of T2DM, the possible hub genes are JUN, VCAM1, RELA, U2AF2, ADRB2, FN1, CDK1, TK1, A2M and ACTA2.. These results could help elucidate the molecular mechanism underlying T2DM pathogenesis and provide potential targets for T2DM therapy. Therefore, more experiments are required to ascertain the clinical value of the identified hub genes as biomarkers and the underlying molecular mechanism.

Acknowledgement

I thank Joan Camunas-Soler, Stanford University, Bioengineering, Quake Lab, Stanford, California, USA, very much, the author who deposited their profiling by high throughput sequencing dataset GSE124742, into the public GEO database.

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. [(GSE124742) (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE124742)]

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. Jing X, Chen J, Dong Y, Han D, Zhao H, Wang X, Gao F, Li C, Cui Z, Liu Y, et al. Related factors of quality of life of type 2 diabetes patients: a systematic review and meta-analysis. Health Qual Life Outcomes. 2018;16(1):189. doi:10.1186/s12955-018-1021-9
2. Moran C, Beare R, Wang W, Callisaya M, Srikanth V; Alzheimer's Disease Neuroimaging Initiative (ADNI). Type 2 diabetes mellitus, brain atrophy, and cognitive decline. Neurology. 2019;92(8):e823-e830. doi:10.1212/WNL.0000000000006955
3. Cannon CP, Perkovic V, Agarwal R, Baldassarre J, Bakris G, Charytan DM, de Zeeuw D, Edwards R, Greene T, Heerspink HJL, et al Evaluating the Effects of Canagliflozin on Cardiovascular and Renal Events in Patients With Type 2 Diabetes Mellitus and Chronic Kidney Disease According to Baseline HbA1c, Including Those With HbA1c <7%: Results From the CREDENCE Trial. Circulation. 2020;141(5):407-410. doi:10.1161/CIRCULATIONAHA.119.044359
4. Choi EY, Park SE, Lee SC, Koh HJ, Kim SS, Byeon SH, Kim M. et al. Association Between Clinical Biomarkers and Optical Coherence Tomography Angiography Parameters in Type 2 Diabetes Mellitus. Invest Ophthalmol Vis Sci. 2020;61(3):4. doi:10.1167/iovs.61.3.4
5. Kenny HC, Abel ED. Heart Failure in Type 2 Diabetes Mellitus. Circ Res. 2019;124(1):121-141. doi:10.1161/CIRCRESAHA.118.311371

6. García-Chapa EG, Leal-Ugarte E, Peralta-Leal V, Durán-González J, Meza-Espinoza JP. Genetic Epidemiology of Type 2 Diabetes in Mexican Mestizos. Biomed Res Int. 2017;2017:3937893. doi:10.1155/2017/3937893
7. Dendup T, Feng X, Clingan S, Astell-Burt T. Environmental Risk Factors for Developing Type 2 Diabetes Mellitus: A Systematic Review. Int J Environ Res Public Health. 2018;15(1):78. doi:10.3390/ijerph15010078
8. Sun Y, Gao HY, Fan ZY, He Y, Yan YX. Metabolomics Signatures in Type 2 Diabetes: A Systematic Review and Integrative Analysis. J Clin Endocrinol Metab. 2020;105(4):dgz240. doi:10.1210/clinem/dgz240
9. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444(7121):840-846. doi:10.1038/nature05482
10. Climie RE, van Sloten TT, Bruno RM, Taddei S, Empana JP, Stehouwer CDA, Sharman JE, Boutouyrie P, Laurent S. Macrovasculature and Microvasculature at the Crossroads Between Type 2 Diabetes Mellitus and Hypertension. Hypertension. 2019;73(6):1138-1149. doi:10.1161/HYPERTENSIONAHA.118.11769
11. Mofo Mato EP, Guewo-Fokeng M, Essop MF, Owira PMO. Genetic polymorphisms of organic cation transporter 1 (OCT1) and responses to metformin therapy in individuals with type 2 diabetes: A systematic review. Medicine (Baltimore). 2018;97(27):e11349. doi:10.1097/MD.0000000000011349
12. Guo X, Li C, Wu J, Mei Q, Liu C, Sun W, Xu L, Fu S. The association of TNF-α -308G/A and -238G/A polymorphisms with type 2 diabetes mellitus: a meta-analysis. Biosci Rep. 2019;39(12):BSR20191301. doi:10.1042/BSR20191301
13. Ding W, Xu L, Zhang L, Han Z, Jiang Q, Wang Z, Jin S. Meta-analysis of association between TCF7L2 polymorphism rs7903146 and type 2 diabetes mellitus. BMC Med Genet. 2018;19(1):38. doi:10.1186/s12881-018-0553-5
14. Rizvi S, Raza ST, Mahdi F, Singh SP, Rajput M, Rahman Q. Genetic polymorphisms in KCNJ11 (E23K, rs5219) and SDF-1β (G801A, rs1801157) genes are associated with the risk of type 2 diabetes mellitus. Br J Biomed Sci. 2018;75(3):139-144. doi:10.1080/09674845.2018.1473939
15. Bregar D, Cilenšek I, Mankoč S, Reschner A, Petrovič D, Globočnik Petrovič M. The joint effect of the endothelin receptor B gene (EDNRB)

polymorphism rs10507875 and nitric oxide synthase 3 gene (NOS3) polymorphism rs869109213 in Slovenian patients with type 2 diabetes mellitus and diabetic retinopathy. Bosn J Basic Med Sci. 2018;18(1):80-86. doi:10.17305/bjbms.2017.2244

16. Huang X, Liu G, Guo J, Su Z. The PI3K/AKT pathway in obesity and type 2 diabetes. Int J Biol Sci. 2018;14(11):1483-1496. doi:10.7150/ijbs.27173
17. Akbari M, Hassan-Zadeh V. IL-6 signalling pathways and the development of type 2 diabetes. Inflammopharmacology. 2018;26(3):685-698. doi:10.1007/s10787-018-0458-0
18. Jin T, Liu L. The Wnt signaling pathway effector TCF7L2 and type 2 diabetes mellitus. Mol Endocrinol. 2008;22(11):2383-2392. doi:10.1210/me.2008-0135
19. Karolina DS, Armugam A, Tavintharan S, et al. MicroRNA 144 impairs insulin signaling by inhibiting the expression of insulin receptor substrate 1 in type 2 diabetes mellitus. PLoS One. 2011;6(8):e22839. doi:10.1371/journal.pone.0022839
20. Zuo Y. The role of adiponectin gene mediated by NF-κB signaling pathway in the pathogenesis of type 2 diabetes. Eur Rev Med Pharmacol Sci. 2018;22(4):1106-1112. doi:10.26355/eurrev_201802_14398
21. Yang F, Chen Y, Xue Z, Lv Y, Shen L, Li K, Zheng P, Pan P, Feng T, Jin L, et al. High-Throughput Sequencing and Exploration of the lncRNA-circRNA-miRNA-mRNA Network in Type 2 Diabetes Mellitus. Biomed Res Int. 2020;2020:8162524. doi:10.1155/2020/8162524
22. Avrahami D, Wang YJ, Schug J, Feleke E, Gao L, Liu C; HPAP Consortium, Naji A, Glaser B, Kaestner KH. Single-cell transcriptomics of human islet ontogeny defines the molecular basis of β-cell dedifferentiation in T2D. Mol Metab. 2020;42:101057. doi:10.1016/j.molmet.2020.101057
23. 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
24. 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
25. 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

26. 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
27. Chen J, Bardes EE, Aronow BJ, Jegga AG. ToppGene Suite for gene list enrichment analysis and candidate gene prioritization. Nucleic Acids Res. 2009;37(Web Server issue):W305-W311. doi:10.1093/nar/gkp427
28. Orchard S, Ammari M, Aranda B, Breuza L, Briganti L, Broackes-Carter F, Campbell NH, Chavali G, Chen C, del-Toro N, et al. The MIntAct project--IntAct as a common curation platform for 11 molecular interaction databases. Nucleic Acids Res. 2014;42(Database issue):D358-D363. doi:10.1093/nar/gkt1115
29. 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
30. 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
31. 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
32. Shi Z, Zhang B. Fast network centrality analysis using GPUs. BMC Bioinformatics. 2011;12:149. doi:10.1186/1471-2105-12-149
33. 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
34. Zaki N, Efimov D, Berengueres J. Protein complex detection using interaction reliability assessment and weighted clustering coefficient. BMC Bioinformatics. 2013;14:163. doi:10.1186/1471-2105-14
35. Fan Y, Xia J (2018) miRNet-Functional Analysis and Visual Exploration of miRNA-Target Interactions in a Network Context. Methods Mol Biol 1819:215-233. doi:10.1007/978-1-4939-8618-7_10
36. Zhou G, Soufan O, Ewald J, Hancock REW, Basu N, Xia J (2019) NetworkAnalyst 3.0: a visual analytics platform for comprehensive gene

expression profiling and meta-analysis. Nucleic Acids Res 47:W234-W241. doi:10.1093/nar/gkz240

37. Robin X, Turck N, Hainard A, Tiberti N, Lisacek F, Sanchez JC, Müller M. pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinformatics 2011;12:77. doi:10.1186/1471-2105-12-77
38. Livak KJ, Schmittgen TD Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. Methods 2001;25:402–408. doi:10.1006/meth.2001.1262
39. Emmens JE, Ter Maaten JM, Damman K, van Veldhuisen DJ, de Boer RA, Struck J, Bergmann A, Sama IE, Streng KW, Anker SD, et al. Proenkephalin, an Opioid System Surrogate, as a Novel Comprehensive Renal Marker in Heart Failure. Circ Heart Fail. 2019;12(5):e005544. doi:10.1161/CIRCHEARTFAILURE.118.005544
40. Wang Y, Cao F, Wang Y, Yu G, Jia BL. Silencing of SAA1 inhibits palmitate- or high-fat diet induced insulin resistance through suppression of the NF-κB pathway. Mol Med. 2019;25(1):17. doi:10.1186/s10020-019-0075-4
41. Du B, Jia X, Tian W, Yan X, Wang N, Cai D, Li X, Zhang H, Jin M, Wu N, et al. Associations of SUCNR1, GRK4, CAMK1D gene polymorphisms and the susceptibility of type 2 diabetes mellitus and essential hypertension in a northern Chinese Han population. J Diabetes Complications. 2021;35(1):107752. doi:10.1016/j.jdiacomp.2020.107752
42. Yeo ES, Hwang JY, Park JE, Choi YJ, Huh KB, Kim WY. Tumor necrosis factor (TNF-alpha) and C-reactive protein (CRP) are positively associated with the risk of chronic kidney disease in patients with type 2 diabetes. Yonsei Med J. 2010;51(4):519-525. doi:10.3349/ymj.2010.51.4.519
43. Scarale MG, Copetti M, Garofolo M, Fontana A, Salvemini L, De Cosmo S, Lamacchia O, Penno G, Trischitta V, Menzaghi C.The Synergic Association of hs-CRP and Serum Amyloid P Component in Predicting All-Cause Mortality in Patients With Type 2 Diabetes. Diabetes Care. 2020;43(5):1025-1032. doi:10.2337/dc19-2489
44. Rees SD, Britten AC, Bellary S, O'Hare JP, Kumar S, Barnett AH, Kelly MA. The promoter polymorphism -232C/G of the PCK1 gene is associated with type 2 diabetes in a UK-resident South Asian population. BMC Med Genet. 2009;10:83. doi:10.1186/1471-2350-10-83

45. Rodriguez S, Eiriksdottir G, Gaunt TR, Harris TB, Launer LJ, Gudnason V, Day IN. IGF2BP1, IGF2BP2 and IGF2BP3 genotype, haplotype and genetic model studies in metabolic syndrome traits and diabetes. Growth Horm IGF Res. 2010;20(4):310-318. doi:10.1016/j.ghir.2010.04.002
46. Luo Y, Qu H, Wang H, Wei H, Wu J, Duan Y, Liu D, Deng H. Plasma Periostin Levels Are Increased in Chinese Subjects with Obesity and Type 2 Diabetes and Are Positively Correlated with Glucose and Lipid Parameters. Mediators Inflamm. 2016;2016:6423637. doi:10.1155/2016/6423637
47. Dankel SN, Svärd J, Matthä S, Claussnitzer M, Klöting N, Glunk V, Fandalyuk Z, Grytten E, Solsvik MH, Nielsen HJ, et al. COL6A3 expression in adipocytes associates with insulin resistance and depends on PPARγ and adipocyte size. Obesity (Silver Spring). 2014;22(8):1807-1813. doi:10.1002/oby.20758
48. Lisa Y, Sook- HF, Yee- HS. Association of the Cocaine- and Amphetamine-Regulated Transcript Prepropeptide Gene (CARTPT) rs2239670 Variant with Obesity among Kampar Health Clinic Patrons, Malaysia. Malays J Med Sci. 2012;19(1):43-51.
49. Nam JS, Ahn CW, Park HJ, Kim YS. Semaphorin 3□C is a Novel Adipokine Representing Exercise-Induced Improvements of Metabolism in Metabolically Healthy Obese Young Males. Sci Rep. 2020;10(1):10005. doi:10.1038/s41598-020-67004-7
50. Poulain-Godefroy O, Eury E, Leloire A, Hennart B, Guillemin GJ, Allorge D, Froguel P.Induction of TDO2 and IDO2 in Liver by High-Fat Feeding in Mice: Discrepancies with Human Obesity. Int J Tryptophan Res. 2013;6(Suppl 1):29-37. doi:10.4137/IJTR.S11717
51. Sun CP, Sun D, Luan ZL, Dai X, Bie X, Ming WH, Sun XW, Huo XX, Lu TL, Zhang D. Association of SOX11 Polymorphisms in distal 3'UTR with Susceptibility for Schizophrenia. J Clin Lab Anal. 2020;34(8):e23306. doi:10.1002/jcla.23306
52. Gorudko IV, Kostevich VA, Sokolov AV, Shamova EV, Buko IV, Konstantinova EE, Vasiliev VB, Cherenkevich SN, Panasenko OM. Functional activity of neutrophils in diabetes mellitus and coronary heart disease: role of myeloperoxidase in the development of oxidative stress. Bull Exp Biol Med. 2012;154(1):23-26. doi:10.1007/s10517-012-1865-7

53. Creely SJ, McTernan PG, Kusminski CM, Fisher fM, Da Silva NF, Khanolkar M, Evans M, Harte AL, Kumar S. Lipopolysaccharide activates an innate immune system response in human adipose tissue in obesity and type 2 diabetes. Am J Physiol Endocrinol Metab. 2007;292(3):E740-E747. doi:10.1152/ajpendo.00302.2006
54. Fateh-Moghadam S, Li Z, Ersel S, Reuter T, Htun P, Plöckinger U, Bocksch W, Dietz R, Gawaz M. Platelet degranulation is associated with progression of intima-media thickness of the common carotid artery in patients with diabetes mellitus type 2. Arterioscler Thromb Vasc Biol. 2005;25(6):1299-1303. doi:10.1161/01.ATV.0000165699.41301.c5
55. Liu JH, Chen Y, Zhen Z, Ho LM, Tsang A, Yuen M, Lam K, Tse HF, Yiu KH. Relationship of biomarkers of extracellular matrix with myocardial function in Type 2 diabetes mellitus. Biomark Med. 2017;11(7):569-578. doi:10.2217/bmm-2017-0044
56. Kundu D, Roy A, Mandal T, Bandyopadhyay U, Ghosh E, Ray D. Relation of microalbuminuria to glycosylated hemoglobin and duration of type 2 diabetes. Niger J Clin Pract. 2013;16(2):216-220. doi:10.4103/1119-3077.110159
57. Suslova TE, Sitozhevskii AV, Ogurkova ON, Kravchenko ES, Kologrivova IV, Anfinogenova Y, Karpov RS. Platelet hemostasis in patients with metabolic syndrome and type 2 diabetes mellitus: cGMP- and NO-dependent mechanisms in the insulin-mediated platelet aggregation. Front Physiol. 2015;5:501. doi:10.3389/fphys.2014.00501
58. Palella E, Cimino R, Pullano SA, Fiorillo AS, Gulletta E, Brunetti A, Foti DP, Greco M. Laboratory Parameters of Hemostasis, Adhesion Molecules, and Inflammation in Type 2 Diabetes Mellitus: Correlation with Glycemic Control. Int J Environ Res Public Health. 2020;17(1):300. doi:10.3390/ijerph17010300
59. Cortez-Navarrete M, Martínez-Abundis E, Pérez-Rubio KG, González-Ortiz M, Méndez-Del Villar M. Momordica charantia Administration Improves Insulin Secretion in Type 2 Diabetes Mellitus. J Med Food. 2018;21(7):672-677. doi:10.1089/jmf.2017.0114
60. Xiao Y, Zheng L, Zou X, Wang J, Zhong J, Zhong T. Extracellular vesicles in type 2 diabetes mellitus: key roles in pathogenesis, complications, and

therapy. J Extracell Vesicles. 2019;8(1):1625677. doi:10.1080/20013078.2019.1625677
61. Saha S. Association between the membrane transporter proteins and type 2 diabetes mellitus. Expert Rev Clin Pharmacol. 2020;13(3):287-297. doi:10.1080/17512433.2020.1729125
62. Hegazy GA, Awan Z, Hashem E, Al-Ama N, Abunaji AB. Levels of soluble cell adhesion molecules in type 2 diabetes mellitus patients with macrovascular complications. J Int Med Res. 2020;48(4):300060519893858. doi:10.1177/0300060519893858
63. Tang X, Hu X, Yang X, Fan Y, Li Y, Hu W, Liao Y, Zheng MC, Peng W, Gao L. Predicting diabetes mellitus genes via protein-protein interaction and protein subcellular localization information. BMC Genomics. 2016;17 Suppl 4(Suppl 4):433. doi:10.1186/s12864-016-2795-y
64. Weijers RN. Lipid composition of cell membranes and its relevance in type 2 diabetes mellitus. Curr Diabetes Rev. 2012;8(5):390-400. doi:10.2174/157339912802083531
65. Nicolle E, Souard F, Faure P, Boumendjel A. Flavonoids as promising lead compounds in type 2 diabetes mellitus: molecules of interest and structure-activity relationship. Curr Med Chem. 2011;18(17):2661-2672. doi:10.2174/092986711795933777
66. Alghamdi F, Guo M, Abdulkhalek S, Crawford N, Amith SR, Szewczuk MR. A novel insulin receptor-signaling platform and its link to insulin resistance and type 2 diabetes. Cell Signal. 2014;26(6):1355-1368. doi:10.1016/j.cellsig.2014.02.015
67. Huang Y, Jin L, Yu H, Jiang G, Tam CHT, Jiang S, Zheng C, Jiang F, Zhang R, Zhang H, et al. SNPs in PRKCA-HIF1A-GLUT1 are associated with diabetic kidney disease in a Chinese Han population with type 2 diabetes. Eur J Clin Invest. 2020;50(9):e13264. doi:10.1111/eci.13264
68. Al-Daghri NM, Al-Attas O, Alokail MS, Alkharfy KM, Draz HM, Agliardi C, Mohammed AK, Guerini FR, Clerici M. Vitamin D receptor gene polymorphisms and HLA DRB1*04 cosegregation in Saudi type 2 diabetes patients. J Immunol. 2012;188(3):1325-1332. doi:10.4049/jimmunol.1101954
69. Zhang S, Sousa A, Lin M, Iwano A, Jain R, Ma B, Lee CM, Park JW, Kamle S, Carlson R, et al. Role of Chitinase 3-Like 1 Protein in the

Pathogenesis of Hepatic Insulin Resistance in Nonalcoholic Fatty Liver Disease. Cells. 2021;10(2):201. doi:10.3390/cells10020201

70. Yamamoto M, Guo DH, Hernandez CM, Stranahan AM. Endothelial Adora2a Activation Promotes Blood-Brain Barrier Breakdown and Cognitive Impairment in Mice with Diet-Induced Insulin Resistance. J Neurosci. 2019;39(21):4179-4192. doi:10.1523/JNEUROSCI.2506-18.2019
71. Connor A, Baumgartner RN, Kerber RA, O'Brien E, Rai SN, Wolff RK, Slattery ML, Giuliano AR, Risendal BC, Byers TE, et al. ADRB2 G-G haplotype associated with breast cancer risk among Hispanic and non-Hispanic white women: interaction with type 2 diabetes and obesity. Cancer Causes Control. 2012;23(10):1653-1663. doi:10.1007/s10552-012-0043-6
72. Cai R, Han J, Sun J, Huang R, Tian S, Shen Y, Dong X, Xia W, Wang S. Plasma Clusterin and the CLU Gene rs11136000 Variant Are Associated with Mild Cognitive Impairment in Type 2 Diabetic Patients. Front Aging Neurosci. 2016;8:179. doi:10.3389/fnagi.2016.00179
73. Woods TC, Satou R, Miyata K, Katsurada A, Dugas CM, Klingenberg NC, Fonseca VA, Navar LG. Canagliflozin Prevents Intrarenal Angiotensinogen Augmentation and Mitigates Kidney Injury and Hypertension in Mouse Model of Type 2 Diabetes Mellitus. Am J Nephrol. 2019;49(4):331-342. doi:10.1159/000499597
74. Nakamura K, Yamagishi S, Adachi H, Matsui T, Kurita-Nakamura Y, Takeuchi M, Inoue H, Imaizumi T. Serum levels of soluble form of receptor for advanced glycation end products (sRAGE) are positively associated with circulating AGEs and soluble form of VCAM-1 in patients with type 2 diabetes. Microvasc Res. 2008;76(1):52-56. doi:10.1016/j.mvr.2007.09.004
75. Bajaj M, Suraamornkul S, Hardies LJ, Glass L, Musi N, DeFronzo RA. Effects of peroxisome proliferator-activated receptor (PPAR)-alpha and PPAR-gamma agonists on glucose and lipid metabolism in patients with type 2 diabetes mellitus. Diabetologia. 2007;50(8):1723-1731. doi:10.1007/s00125-007-0698-9
76. Chan GC, Divers J, Russell GB, Langefeld CD, Wagenknecht LE, Hsu FC, Xu J, Smith SC, Palmer ND, Hicks PJ, et al. FGF23 Concentration and APOL1 Genotype Are Novel Predictors of Mortality in African Americans With Type 2 Diabetes. Diabetes Care. 2018;41(1):178-186. doi:10.2337/dc17-0820

77. Caracciolo V, Young J, Gonzales D, Ni Y, Flowers SJ, Summer R, Waldman SA, Kim JK, Jung DY, Noh HL, et al. Myeloid-specific deletion of Zfp36 protects against insulin resistance and fatty liver in diet-induced obese mice. Am J Physiol Endocrinol Metab. 2018;315(4):E676-E693. doi:10.1152/ajpendo.00224.2017
78. Wu YS, Li ZM, Chen YT, Dai SJ, Zhou XJ, Yang YX, Lou JS, Ji LT, Bao YT, Xuan L, et al. Berberine Improves Inflammatory Responses of Diabetes Mellitus in Zucker Diabetic Fatty Rats and Insulin-Resistant HepG2 Cells through the PPM1B Pathway. J Immunol Res. 2020;2020:2141508. doi:10.1155/2020/2141508
79. Opazo-Ríos L, Sanchez Matus Y, Rodrigues-Díez RR, Carpio D, Droguett A, Egido J, Gomez-Guerrero C, Mezzano S.Anti-inflammatory, antioxidant and renoprotective effects of SOCS1 mimetic peptide in the BTBR ob/ob mouse model of type 2 diabetes. BMJ Open Diabetes Res Care. 2020;8(1):e001242. doi:10.1136/bmjdrc-2020-001242
80. Hong CT, Chen KY, Wang W, Chiu JY, Wu D, Chao TY, Hu CJ, Chau KD, Bamodu OA. Insulin Resistance Promotes Parkinson's Disease through Aberrant Expression of α-Synuclein, Mitochondrial Dysfunction, and Deregulation of the Polo-Like Kinase 2 Signaling. Cells. 2020;9(3):740. doi:10.3390/cells9030740
81. Wen W, Sun H, Yang Y, Jia Y, Fang F, Qin Y, Zhang M, Wei Y. Usefulness of Cathepsin S to Predict Risk for Obstructive Sleep Apnea among Patients with Type 2 Diabetes. Dis Markers. 2020;2020:8819134. doi:10.1155/2020/8819134
82. Wu X, Yu T, Ji N, Huang Y, Gao L, Shi W, Yan Y, Li H, Ma L, Wu K, et al. IL6R inhibits viability and apoptosis of pancreatic beta-cells in type 2 diabetes mellitus via regulation by miR-22 of the JAK/STAT signaling pathway. Diabetes Metab Syndr Obes. 2019;12:1645-1657. doi:10.2147/DMSO.S211700
83. Wang J, Yang MM, Li YB, Liu GD, Teng Y, Liu XM. Association of CFH and CFB gene polymorphisms with retinopathy in type 2 diabetic patients. Mediators Inflamm. 2013;2013:748435. doi:10.1155/2013/748435
84. Soraia Aguiar de Melo Dias R, Carlos Mourão Pinho R, Almeida FR, Alfredo Farias Bandeira F, Celerino da Silva R, Crovella S, de Carvalho Farias Vajgel B, Cimões R. Evaluation of DEFB1 polymorphisms in

individuals with chronic periodontitis and diabetes mellitus type 2 in a population of northeastern Brazil. Spec Care Dentist. 2018;38(4):227-233. doi:10.1111/scd.12296

85. van Diepen JA, Jansen PA, Ballak DB, Hijmans A, Rutjes FP, Tack CJ, Netea MG, Schalkwijk J, Stienstra R. Genetic and pharmacological inhibition of vanin-1 activity in animal models of type 2 diabetes. Sci Rep. 2016;6:21906. Published 2016 Mar 2. doi:10.1038/srep21906
86. Jiang S, Shen D, Jia WJ, Han X, Shen N, Tao W, Gao X, Xue B, Li CJ. GGPPS-mediated Rab27A geranylgeranylation regulates β cell dysfunction during type 2 diabetes development by affecting insulin granule docked pool formation. J Pathol. 2016;238(1):109-119. doi:10.1002/path.4652
87. Lee SA, Kim YR, Yang EJ, Kwon EJ, Kim SH, Kang SH, Park DB, Oh BC, Kim J, Heo ST, et al. CD26/DPP4 levels in peripheral blood and T cells in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab. 2013;98(6):2553-2561. doi:10.1210/jc.2012-4288
88. Zhao K, Ding W, Zhang Y, Ma K, Wang D, Hu C, Liu J, Zhang X. Variants in the RARRES2 gene are associated with serum chemerin and increase the risk of diabetic kidney disease in type 2 diabetes. Int J Biol Macromol. 2020;165(Pt A):1574-1580. doi:10.1016/j.ijbiomac.2020.10.030
89. Vincent JA, Mohr S. Inhibition of caspase-1/interleukin-1beta signaling prevents degeneration of retinal capillaries in diabetes and galactosemia. Diabetes. 2007;56(1):224-230. doi:10.2337/db06-0427
90. Wang W, Ye S, Qian L, Xing Y, Ren A, Chen C, Li S, Xu J, Liu Q, Dong L, et al. Elevated serum lipocalin 2 levels are associated with indexes of both glucose and bone metabolism in type 2 diabetes mellitus. Endokrynol Pol. 2018;69(3):276-282. doi:10.5603/EP.a2018.0030
91. Wu Y, Quan Y, Liu Y, Liu K, Li H, Jiang Z, Zhang T, Lei H, Radek KA, Li D, et al. Hyperglycaemia inhibits REG3A expression to exacerbate TLR3-mediated skin inflammation in diabetes. Nat Commun. 2016;7:13393. doi:10.1038/ncomms13393
92. Chan PC, Wu TN, Chen YC, Lu CH, Wabitsch M, Tian YF, Hsieh PS. Targetted inhibition of CD74 attenuates adipose COX-2-MIF-mediated M1 macrophage polarization and retards obesity-related adipose tissue inflammation and insulin resistance. Clin Sci (Lond). 2018;132(14):1581-1596. doi:10.1042/CS20180041

93. Chang TJ, Chiu YF, Sheu WH, Shih KC, Hwu CM, Quertermous T, Jou YS, Kuo SS, et al. Genetic polymorphisms of PCSK2 are associated with glucose homeostasis and progression to type 2 diabetes in a Chinese population. Sci Rep. 2015;5:14380. doi:10.1038/srep14380
94. Herold Z, Herold M, Rosta K, Doleschall M, Somogyi A. Lower serum chromogranin B level is associated with type 1 diabetes and with type 2 diabetes patients with intensive conservative insulin treatment. Diabetol Metab Syndr. 2020;12:61. doi:10.1186/s13098-020-00569-5
95. Kwanbunjan K, Panprathip P, Phosat C, Chumpathat N, Wechjakwen N, Puduang S, Auyyuenyong R, Henkel I, Schweigert FJ. Association of retinol binding protein 4 and transthyretin with triglyceride levels and insulin resistance in rural thais with high type 2 diabetes risk. BMC Endocr Disord. 2018;18(1):26. doi:10.1186/s12902-018-0254-2
96. Liu JJ, Pek SLT, Wang J, Liu S, Ang K, Shao YM, Tang JI, Gurung RL, Tavintharan S, Tang WE, et al. Association of Plasma Leucine-Rich α-2 Glycoprotein 1, a Modulator of Transforming Growth Factor-β Signaling Pathway, With Incident Heart Failure in Individuals With Type 2 Diabetes. Diabetes Care. 2021;44(2):571-577. doi:10.2337/dc20-2065
97. Hu F, Lou Y, Shi J, Cao L, Wang C, Ma J, Peng X, Xu S, Chen H, Zhao D et al. Baseline serum albumin and its dynamic change is associated with type 2 diabetes risk: A large cohort study in China. Diabetes Metab Res Rev. 2020;36(5):e3296. doi:10.1002/dmrr.3296
98. Makrilakis K. The Role of DPP-4 Inhibitors in the Treatment Algorithm of Type 2 Diabetes Mellitus: When to Select, What to Expect. Int J Environ Res Public Health. 2019;16(15):2720. doi:10.3390/ijerph16152720
99. Castro A, Lázaro I, Selva DM, Céspedes E, Girona J, NúriaPlana, Guardiola M, Cabré A, Simó R, Masana L. APOH is increased in the plasma and liver of type 2 diabetic patients with metabolic syndrome. Atherosclerosis. 2010;209(1):201-205. doi:10.1016/j.atherosclerosis.2009.09.072
100. Ding L, Houben T, Oligschlaeger Y, Bitorina AV, Verwer BJ, Tushuizen ME, Shiri-Sverdlov R. Plasma Cathepsin D Activity Rather Than Levels Correlates With Metabolic Parameters of Type 2 Diabetes in Male Individuals. Front Endocrinol (Lausanne). 2020;11:575070. doi:10.3389/fendo.2020.575070

101. Li L, Gao K, Zhao J, Feng T, Yin L, Wang J, Wang C, Li C, Wang Y, Wang Q, et al. Glucagon gene polymorphism modifies the effects of smoking and physical activity on risk of type 2 diabetes mellitus in Han Chinese. Gene. 2014;534(2):352-355. doi:10.1016/j.gene.2013.09.121
102. Travers ME, Mackay DJ, Dekker Nitert M, Morris AP, Lindgren CM, Berry A, Johnson PR, Hanley N, Groop LC, McCarthy MI, et al. Insights into the molecular mechanism for type 2 diabetes susceptibility at the KCNQ1 locus from temporal changes in imprinting status in human islets. Diabetes. 2013;62(3):987-992. doi:10.2337/db12-0819
103. Ming Y, Yin Y, Sun Z. Interaction of Nuclear Receptor Subfamily 4 Group A Member 1 (Nr4a1) and Liver Linase B1 (LKB1) Mitigates Type 2 Diabetes Mellitus by Activating Monophosphate-Activated Protein Kinase (AMPK)/Sirtuin 1 (SIRT1) Axis and Inhibiting Nuclear Factor-kappa B (NF-κB) Activation. Med Sci Monit. 2020;26:e920278.. doi:10.12659/MSM.920278
104. Gemmink A, Daemen S, Brouwers B, Huntjens PR, Schaart G, Moonen-Kornips E, Jörgensen J, Hoeks J, Schrauwen P, Hesselink MKC. Dissociation of intramyocellular lipid storage and insulin resistance in trained athletes and type 2 diabetes patients; involvement of perilipin 5?. J Physiol. 2018;596(5):857-868. doi:10.1113/JP275182
105. Li GY, Li ZB, Li F, Dong LP, Tang L, Xiang J, Li JM, Bao MH. Meta-Analysis on the Association of ALDH2 Polymorphisms and Type 2 Diabetic Mellitus, Diabetic Retinopathy. Int J Environ Res Public Health. 2017;14(2):165. doi:10.3390/ijerph14020165
106. Siebert J, Reiwer-Gostomska M, Mysliwska J, Marek N, Raczynska K, Glasner L. Glycemic control influences serum angiogenin concentrations in patients with type 2 diabetes. Diabetes Care. 2010;33(8):1829-1830. doi:10.2337/dc10-0130
107. Belalcazar LM, Papandonatos GD, McCaffery JM, Peter I, Pajewski NM, Erar B, Allred ND, Balasubramanyam A, Bowden DW, Brautbar A, et al. A common variant in the CLDN7/ELP5 locus predicts adiponectin change with lifestyle intervention and improved fitness in obese individuals with diabetes. Physiol Genomics. 2015;47(6):215-224. doi:10.1152/physiolgenomics.00109.2014

108. Erdenebaatar C, Yamaguchi M, Monsur M, Saito F, Honda R, Tashiro H, Ohba T, Iyama KI, Katabuchi H. Serum Prolactin Contributes to Enhancing Prolactin Receptor and pJAK2 in Type I Endometrial Cancer Cells in Young Women Without Insulin Resistance. Int J Gynecol Pathol. 2019;38(4):318-325. doi:10.1097/PGP.0000000000000527
109. Işikli A, Kubat-Üzüm A, Satman İ, Matur Z, Öge AE, Küçükali Cİ, Tüzün E, Erden S, Özkök E. A SOD2 Polymorphism is Associated with Abnormal Quantitative Sensory Testing in Type 2 Diabetic Patients. Noro Psikiyatr Ars. 2018;55(3):276-279. doi:10.29399/npa.23027
110. Mtiraoui N, Turki A, Nemr R, Echtay A, Izzidi I, Al-Zaben GS, Irani-Hakime N, Keleshian SH, Mahjoub T, Almawi WY. Contribution of common variants of ENPP1, IGF2BP2, KCNJ11, MLXIPL, PPARγ, SLC30A8 and TCF7L2 to the risk of type 2 diabetes in Lebanese and Tunisian Arabs. Diabetes Metab. 2012;38(5):444-449. doi:10.1016/j.diabet.2012.05.002
111. Ding L, Houben T, Oligschlaeger Y, Bitorina AV, Verwer BJ, Tushuizen ME, Shiri-Sverdlov R. Plasma Cathepsin D. Plasma Cathepsin D Activity Rather Than Levels Correlates With Metabolic Parameters of Type 2 Diabetes in Male Individuals. Front Endocrinol (Lausanne). 2020;11:575070. doi:10.3389/fendo.2020.575070
112. Završnik M, Kariž S, Makuc J, Šeruga M, Cilenšek I, Petrovič D. PECAM-1 Leu125Val (rs688) Polymorphism and Diabetic Nephropathy in Caucasians with Type 2 Diabetes Mellitus. Anal Cell Pathol (Amst). 2016;2016:3152967. doi:10.1155/2016/3152967
113. Niraula A, Thapa S, Kunwar S, Lamsal M, Baral N, Maskey R. Adenosine deaminase activity in type 2 diabetes mellitus: does it have any role?. BMC Endocr Disord. 2018;18(1):58. doi:10.1186/s12902-018-0284-9
114. Sun G, Liu J, Xia G, Zhang L, Li Y, Zhou Z, Lv Y, Wei S, Liu J, Quan J. Reduced serum milk fat globule-epidermal growth factor 8 (MFG-E8) concentrations are associated with an increased risk of microvascular complications in patients with type 2 diabetes. Clin Chim Acta. 2017;466:201-206. doi:10.1016/j.cca.2017.01.013
115. Lin G, Wan X, Liu D, Wen Y, Yang C, Zhao C. COL1A1 as a potential new biomarker and therapeutic target for type 2 diabetes. Pharmacol Res. 2021;105436. doi:10.1016/j.phrs.2021.105436

116. Gaikwad AB, Gupta J, Tikoo K. Epigenetic changes and alteration of Fbn1 and Col3A1 gene expression under hyperglycaemic and hyperinsulinaemic conditions. Biochem J. 2010;432(2):333-341. doi:10.1042/BJ20100414
117. Sasso FC, Marfella R, Pagano A, Porta G, Signoriello G, Lascar N, Minutolo R, Carbonara O, Persico M, Piscione F, et al. Lack of effect of aspirin in primary CV prevention in type 2 diabetic patients with nephropathy: results from 8 years follow-up of NID-2 study. Acta Diabetol. 2015;52(2):239-247. doi:10.1007/s00592-014-0623-x
118. Fawad Ali Shah S, Iqbal T, Naveed N, Akram S, Arshad Rafiq M, Hussain S. ARG1 single nucleotide polymorphisms rs2781666 and rs2781665 confer risk of Type 2 diabetes mellitus. EXCLI J. 2018;17:847-855. doi:10.17179/excli2018-1178
119. Lee M, Park HS, Choi MY, Kim HZ, Moon SJ, Ha JY, Choi A, Park YW, Park JS, Shin EC, et al. Significance of Soluble CD93 in Type 2 Diabetes as a Biomarker for Diabetic Nephropathy: Integrated Results from Human and Rodent Studies. J Clin Med. 2020;9(5):1394. doi:10.3390/jcm9051394
120. Mercader JM, Liao RG, Bell AD, Dymek Z, Estrada K, Tukiainen T, Huerta-Chagoya A, Moreno-Macías H, Jablonski KA, Hanson RL, et al. A Loss-of-Function Splice Acceptor Variant in IGF2 Is Protective for Type 2 Diabetes. Diabetes. 2017;66(11):2903-2914. doi:10.2337/db17-018
121. Hivert MF, Sun Q, Shrader P, Mantzoros CS, Meigs JB, Hu FB. Circulating IL-18 and the risk of type 2 diabetes in women. Diabetologia. 2009;52(10):2101-2108. doi:10.1007/s00125-009-1455-z
122. Perry JR, Voight BF, Yengo L, Amin N, Dupuis J, Ganser M, Grallert H, Navarro P, Li M, Qi L, et al. Yengo L, et al. Stratifying type 2 diabetes cases by BMI identifies genetic risk variants in LAMA1 and enrichment for risk variants in lean compared to obese cases. PLoS Genet. 2012;8(5):e1002741. doi:10.1371/journal.pgen.1002741
123. Simeonovic CJ, Ziolkowski AF, Wu Z, Choong FJ, Freeman C, Parish CR. Heparanase and autoimmune diabetes. Front Immunol. 2013;4:471. doi:10.3389/fimmu.2013.00471
124. Youn JY, Zhou J, Cai H. Bone Morphogenic Protein 4 Mediates NOX1-Dependent eNOS Uncoupling, Endothelial Dysfunction, and COX2

Induction in Type 2 Diabetes Mellitus. Mol Endocrinol. 2015;29(8):1123-1133. doi:10.1210/ME.2014-1313

125. Vidaković M, Grdović N, Dinić S, Mihailović M, Uskoković A, Arambašić Jovanović J. The Importance of the CXCL12/CXCR4 Axis in Therapeutic Approaches to Diabetes Mellitus Attenuation. Front Immunol. 2015;6:403. doi:10.3389/fimmu.2015.00403

126. Merlo S, Starčević JN, Mankoč S, Šantl Letonja M, Cokan Vujkovac A, Zorc M, Petrovič D. Vascular Endothelial Growth Factor Gene Polymorphism (rs2010963) and and Its Receptor, Kinase Insert Domain-Containing Receptor Gene Polymorphism (rs2071559), and Markers of Carotid Atherosclerosis in Patients with Type 2 Diabetes Mellitus. J Diabetes Res. 2016;2016:1482194. doi:10.1155/2016/1482194

127. Kacso IM, Potra AR, Rusu A, Moldovan D, Rusu CC, Kacso G, Hancu ND, Muresan A, Bondor CI. su A, et al. Relationship of endothelial cell selective adhesion molecule to markers of oxidative stress in type 2 diabetes. Scand J Clin Lab Invest. 2014;74(2):170-176. doi:10.3109/00365513.2013.869700

128. Bai J, Xia M, Xue Y, Ma F, Cui A, Sun Y, Han Y, Xu X, Zhang F, Hu Z, et al. Thrombospondin 1 improves hepatic steatosis in diet-induced insulin-resistant mice and is associated with hepatic fat content in humans. EBioMedicine. 2020;57:102849. doi:10.1016/j.ebiom.2020.102849

129. Yamashita A, Nishihira K, Matsuura Y, Ito T, Kawahara K, Hatakeyama K, Hashiguchi T, Maruyama I, Yagi H, Matsumoto M, et al. Paucity of CD34-positive cells and increased expression of high-mobility group box 1 in coronary thrombus with type 2 diabetes mellitus. Atherosclerosis. 2012;224(2):511-514. doi:10.1016/j.atherosclerosis.2012.07.027

130. Fan Q, Li H, Qin Y, Li L, Chen L, Zhang L, Lv Y, Liang D, Liang Y, Long T, et al. Association of SERPINE1 rs6092 with type 2 diabetes and related metabolic traits in a Chinese population. Gene. 2018;661:176-181. doi:10.1016/j.gene.2018.04.011

131. Salpea KD, Gable DR, Cooper JA, Stephens JW, Hurel SJ, Ireland HA, Feher MD, Godsland IF, Humphries SE. The effect of WNT5B IVS3C>G on the susceptibility to type 2 diabetes in UK Caucasian subjects.

Nutr Metab Cardiovasc Dis. 2009;19(2):140-145. doi:10.1016/j.numecd.2008.02.009

132. Sardana M, Vasim I, Varakantam S, Kewan U, Tariq A, Koppula MR, Syed AA, Beraun M, Drummen NE, Vermeer C, et al. Inactive Matrix Gla-Protein and Arterial Stiffness in Type 2 Diabetes Mellitus. Am J Hypertens. 2017;30(2):196-201. doi:10.1093/ajh/hpw146

133. Lee JE, Choi YK, Seo HA, Jeon JH, Jeong JY, Moon SS, Kim JG, Kim BW, Kim SW, Min Yoo, et al. Impact of ENPP1 and MMP3 gene polymorphisms on aortic calcification in patients with type 2 diabetes in a Korean population. Diabetes Res Clin Pract. 2010;88(1):87-96. doi:10.1016/j.diabres.2010.01.002

134. 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

135. Arcidiacono B, Chiefari E, Laria AE, Messineo S, Bilotta FL, Britti D, Foti DP, Foryst-Ludwig A, Kintscher U, Brunetti A. Expression of matrix metalloproteinase-11 is increased under conditions of insulin resistance. World J Diabetes. 2017;8(9):422-428. doi:10.4239/wjd.v8.i9.422

136. Cheng F, Liu L, Zhang H, Zhu Y, Li X, Li H. Association of IL-16 gene polymorphisms with the risk of developing type 2 diabetes mellitus in the Chinese Han population. Biosci Rep. 2019;39(8):BSR20190821. doi:10.1042/BSR20190821

137. Biscetti F, Porreca CF, Bertucci F, Straface G, Santoliquido A, Tondi P, Angelini F, Pitocco D, Santoro L, Gasbarrini A, et al. TNFRSF11B gene polymorphisms increased risk of peripheral arterial occlusive disease and critical limb ischemia in patients with type 2 diabetes. Acta Diabetol. 2014;51(6):1025-1032. doi:10.1007/s00592-014-0664-1

138. Jiang C, Xia W, Wu T, Pan C, Shan H, Wang F, Zhou Z, Yu X. Inhibition of microRNA-222 up-regulates TIMP3 to promotes osteogenic differentiation of MSCs from fracture rats with type 2 diabetes mellitus. J Cell Mol Med. 2020;24(1):686-694. doi:10.1111/jcmm.14777

139. Walder K, McMillan J, Lapsys N, Kriketos A, Trevaskis J, Civitarese A, Southon A, Zimmet P, Collier G. Calpain 3 gene expression in skeletal muscle is associated with body fat content and measures of insulin

resistance. Int J Obes Relat Metab Disord. 2002;26(4):442-449. doi:10.1038/sj.ijo.0801946

140. Howson JM, Walker NM, Clayton D, Todd JA; Type 1 Diabetes Genetics Consortium. Confirmation of HLA class II independent type 1 diabetes associations in the major histocompatibility complex including HLA-B and HLA-A. Diabetes Obes Metab. 2009;11 Suppl 1(Suppl 1):31-45. doi:10.1111/j.1463-1326.2008.01001.x

141. Schloss J, Ali R, Racine JJ, Chapman HD, Serreze DV, DiLorenzo TP. HLA-B*39:06 Efficiently Mediates Type 1 Diabetes in a Mouse Model Incorporating Reduced Thymic Insulin Expression. J Immunol. 2018;200(10):3353-3363. doi:10.4049/jimmunol.1701652

142. Zhi D, Sun C, Sedimbi SK, Luo F, Shen S, Sanjeevi CB. Killer cell immunoglobulin-like receptor along with HLA-C ligand genes are associated with type 1 diabetes in Chinese Han population. Diabetes Metab Res Rev. 2011;27(8):872-877. doi:10.1002/dmrr.1264

143. Varney MD, Valdes AM, Carlson JA, Noble JA, Tait BD, Bonella P, Lavant E, Fear AL, Louey A, Moonsamy P, et al. HLA DPA1, DPB1 alleles and haplotypes contribute to the risk associated with type 1 diabetes: analysis of the type 1 diabetes genetics consortium families. Diabetes. 2010;59(8):2055-2062. doi:10.2337/db09-0680

144. Jiang H, Canfield SM, Gallagher MP, Jiang HH, Jiang Y, Zheng Z, Chess L. HLA-E-restricted regulatory CD8(+) T cells are involved in development and control of human autoimmune type 1 diabetes. J Clin Invest. 2010;120(10):3641-3650. doi:10.1172/JCI4352

145. Wang D, Pan G. The Association between rs2292239 Polymorphism in ERBB3 Gene and Type 1 Diabetes: A Meta-Analysis. Biomed Res Int. 2019;2019:7689642. doi:10.1155/2019/7689642

146. Blindbæk SL, Schlosser A, Green A, Holmskov U, Sorensen GL, Grauslund J. Association between microfibrillar-associated protein 4 (MFAP4) and micro- and macrovascular complications in long-term type 1 diabetes mellitus. Acta Diabetol. 2017;54(4):367-372. doi:10.1007/s00592-016-0953-y

147. Cetkovic-Cvrlje M, Dragt AL, Vassilev A, Liu XP, Uckun FM. Targeting JAK3 with JANEX-1 for prevention of autoimmune type 1

diabetes in NOD mice. Clin Immunol. 2003;106(3):213-225. doi:10.1016/s1521-6616(02)00049-9

148. Li J, Jian L, Huang J, Xiong N, Wang T. The rs3129882/rs4248166 in HLA-DRA and rs34372695 in SYT11 are not associated with sporadic Parkinson's disease in Central Chinese population. Int J Neurosci. 2020;1-7. doi:10.1080/00207454.2020.1753728

149. Halbgebauer S, Nagl M, Klafki H, Haußmann U, Steinacker P, Oeckl P, Kassubek J, Pinkhardt E, Ludolph AC, Soininen H, et al. Modified serpinA1 as risk marker for Parkinson's disease dementia: Analysis of baseline data. Sci Rep. 2016;6:26145. doi:10.1038/srep26145

150. Ichu TA, Reed A, Ogasawara D, Ulanovskaya O, Roberts A, Aguirre CA, Bar-Peled L, Gao J, Germain J, Barbas S, et al. ABHD12 and LPCAT3 Interplay Regulates a Lyso-phosphatidylserine-C20:4 Phosphatidylserine Lipid Network Implicated in Neurological Disease. Biochemistry. 2020;59(19):1793-1799. doi:10.1021/acs.biochem.0c00292

151. Bloch PJ, Weller AE, Doyle GA, Ferraro TN, Berrettini WH, Hodge R, Lohoff FW. Association analysis between polymorphisms in the myo-inositol monophosphatase 2 (IMPA2) gene and bipolar disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2010;34(8):1515-1519. doi:10.1016/j.pnpbp.2010.08.015

152. Yoo HS, Lee JS, Chung SJ, Ye BS, Sohn YH, Lee SJ, Lee PH. Changes in plasma arylsulfatase A level as a compensatory biomarker of early Parkinson's disease. Sci Rep. 2020;10(1):5567. doi:10.1038/s41598-020-62536-4

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. Han Q, Sun YA, Zong Y, Chen C, Wang HF, Tan L. Common Variants in PLXNA4 and Correlation to CSF-related Phenotypes in Alzheimer's Disease. Front Neurosci. 2018;12:946. doi:10.3389/fnins.2018.00946

155. Yang CR, Ning L, Zhou FH, Sun Q, Meng HP, Han Z, Liu Y, Huang W, Liu S, Li XH, et al. Downregulation of Adhesion Molecule CHL1 in B

Cells but Not T Cells of Patients with Major Depression and in the Brain of Mice with Chronic Stress. Neurotox Res. 2020;38(4):914-928. doi:10.1007/s12640-020-00234-9

156. Stygelbout V, Leroy K, Pouillon V, Ando K, D'Amico E, Jia Y, Luo HR, Duyckaerts C, Erneux C, Schurmans S, et al. on V, et al. Inositol trisphosphate 3-kinase B is increased in human Alzheimer brain and exacerbates mouse Alzheimer pathology. Brain. 2014;137(Pt 2):537-552. doi:10.1093/brain/awt344

157. Alguacil LF, Herradón G. Midkine and Pleiotrophin in the Treatment of Neurodegenerative Diseases and Drug Addiction. Recent Pat CNS Drug Discov. 2015;10(1):28-33. doi:10.2174/1574889810666150326103916

158. Ahmad S, Milan MDC, Hansson O, Demirkan A, Agustin R, Sáez ME, Giagtzoglou N, Cabrera-Socorro A, Bakker MHM, Ramirez A, et al. CDH6 and HAGH protein levels in plasma associate with Alzheimer's disease in APOE ε4 carriers. Sci Rep. 2020;10(1):8233. doi:10.1038/s41598-020-65038-5

159. Arreguin AJ, Colognato H. Brain Dysfunction in LAMA2-Related Congenital Muscular Dystrophy: Lessons From Human Case Reports and Mouse Models. Front Mol Neurosci. 2020;13:118. doi:10.3389/fnmol.2020.00118

160. Bruno E, Quattrocchi G, Nicoletti A, Le Pira F, Maci T, Mostile G, Andreoli V, Quattrone A, Zappia M. Lack of interaction between LRP1 and A2M polymorphisms for the risk of Alzheimer disease. Neurosci Lett. 2010;482(2):112-116. doi:10.1016/j.neulet.2010.07.012

161. Zidi I, Kharrat N, Abdelhedi R, Hassine AB, Laaribi AB, Yahia HB, Abdelmoula NB, Abid L, Rebai A, Rizzo R. Nonclassical human leukocyte antigen (HLA-G, HLA-E, and HLA-F) in coronary artery disease. Hum Immunol. 2016;77(4):325-329. doi:10.1016/j.humimm.2016.01.008

162. Annichino-Bizzacchi JM, Saad ST, Arruda VR, Ramires JA, Siqueira LH, Chiaparini LC, Mansur AP. C282Y mutation in the HLA-H gene is not a risk factor for patients with myocardial infarction. J Cardiovasc Risk. 2000;7(1):37-40. doi:10.1177/204748730000700107

163. Jacquemin B, Antoniades C, Nyberg F, Plana E, Müller M, Greven S, Salomaa V, Sunyer J, Bellander T, Chalamandaris AG, et al. Common genetic polymorphisms and haplotypes of fibrinogen alpha, beta, and gamma

chains affect fibrinogen levels and the response to proinflammatory stimulation in myocardial infarction survivors: the AIRGENE study. J Am Coll Cardiol. 2008;52(11):941-952. doi:10.1016/j.jacc.2008.06.016

164. Yang Z, Zhang Q, Yu H, Du H, Li L, He Y, Zhu S, Li C, Zhang S, Luo B, et al. Genetic association study of a novel indel polymorphism in HSPA1B with the risk of sudden cardiac death in the Chinese populations. Forensic Sci Int. 2021;318:110637. doi:10.1016/j.forsciint.2020.110637

165. Yarnazari A, Hassanpour P, Hosseini-Fard SR, Amirfarhangi A, Najafi M. The sdLDL Reduces MRC1 Expression Level and Secretion of Histamin e in Differentiated M2-macrophages from Patients with Coronary Artery Stenosis. Cardiovasc Hematol Disord Drug Targets. 2017;17(1):28-32. doi:10.2174/1871529X17666170106095554

166. Harrison SC, Cooper JA, Li K, Talmud PJ, Sofat R, Stephens JW, Hamsten A; HIFMECH Consortium, Sanders J, Montgomery H, Neil A; Simon Broome Research Consortium, Humphries SE. Association of a sequence variant in DAB2IP with coronary heart disease. Eur Heart J. 2012;33(7):881-888. doi:10.1093/eurheartj/ehr075

167. Delaney JT, Muhammad R, Blair MA, Kor K, Fish FA, Roden DM, Darbar D. A KCNJ8 mutation associated with early repolarization and atrial fibrillation. Europace. 2012;14(10):1428-1432. doi:10.1093/europace/eus150

168. Gittleman HR, Merkulova A, Alhalabi O, Stavrou EX, Veigl ML, Barnholtz-Sloan JS, Schmaier AH. A Cross-sectional Study of KLKB1 and PRCP Polymorphisms in Patient Samples with Cardiovascular Disease. Front Med (Lausanne). 2016;3:17. doi:10.3389/fmed.2016.00017

169. Guo LY, Yang F, Peng LJ, Li YB, Wang AP. CXCL2, a new critical factor and therapeutic target for cardiovascular diseases. Clin Exp Hypertens. 2020;42(5):428-437. doi:10.1080/10641963.2019.1693585

170. Li X, Zhao D, Guo Z, Li T, Qili M, Xu B, Qian M, Liang H, E X, Chege Gitau S, Wang L, et al. Overexpression of SerpinE2/protease nexin-1 Contribute to Pathological Cardiac Fibrosis via increasing Collagen Deposition. Sci Rep. 2016;6:37635. doi:10.1038/srep37635

171. Latella MC, Di Castelnuovo A, de Lorgeril M, Arnout J, Cappuccio FP, Krogh V, Siani A, van Dongen M, Donati MB, de Gaetano G, et al. Genetic variation of alcohol dehydrogenase type 1C (ADH1C), alcohol

consumption, and metabolic cardiovascular risk factors: results from the IMMIDIET study. Atherosclerosis. 2009;207(1):284-290. doi:10.1016/j.atherosclerosis.2009.04.022

172. Liu H, Luo D, Qiu Y, Huang Y, Chen C, Song X, Gao L, Zhou Y. The Effect of AMBP SNPs, Their Haplotypes, and Gene-Environment Interactions on the Risk of Atherothrombotic Stroke Among the Chinese Population. Genet Test Mol Biomarkers. 2019;23(7):487-494. doi:10.1089/gtmb.2018.0248

173. Kardys I, van Tiel CM, de Vries CJ, Pannekoek H, Uitterlinden AG, Hofman A, Witteman JC, de Maat MP. Haplotypes of the NR4A2/NURR1 gene and cardiovascular disease: the Rotterdam Study. Hum Mutat. 2009;30(3):417-423. doi:10.1002/humu.20902

174. Li W, Yue H. Thymidine phosphorylase: A potential new target for treating cardiovascular disease. Trends Cardiovasc Med. 2018;28(3):157-171. doi:10.1016/j.tcm.2017.10.003

175. Xu W, Barrientos T, Mao L, Rockman HA, Sauve AA, Andrews NC. Lethal Cardiomyopathy in Mice Lacking Transferrin Receptor in the Heart. Cell Rep. 2015;13(3):533-545. doi:10.1016/j.celrep.2015.09.023

176. Persson M, Engström G, Björkbacka H, Hedblad B. Soluble urokinase plasminogen activator receptor in plasma is associated with incidence of CVD. Results from the Malmö Diet and Cancer Study. Atherosclerosis. 2012;220(2):502-505. doi:10.1016/j.atherosclerosis.2011.10.039

177. Grossman TR, Gamliel A, Wessells RJ, Taghli-Lamallem O, Jepsen K, Ocorr K, Korenberg JR, Peterson KL, Rosenfeld MG, Bodmer R, et al. Over-expression of DSCAM and COL6A2 cooperatively generates congenital heart defects. PLoS Genet. 2011;7(11):e1002344. doi:10.1371/journal.pgen.1002344

178. Connelly JJ, Cherepanova OA, Doss JF, Karaoli T, Lillard TS, Markunas CA, Nelson S, Wang T, Ellis PD, Langford CF, et al. Epigenetic regulation of COL15A1 in smooth muscle cell replicative aging and atherosclerosis. Hum Mol Genet. 2013;22(25):5107-5120. doi:10.1093/hmg/ddt365

179. Delfín DA, DeAguero JL, McKown EN. The Extracellular Matrix Protein ABI3BP in Cardiovascular Health and Disease. Front Cardiovasc Med. 2019;6:23. doi:10.3389/fcvm.2019.00023

180. Hu YW, Guo FX, Xu YJ, Li P, Lu ZF, McVey DG, Zheng L, Wang Q, Ye JH, Kang CM, et al. Long noncoding RNA NEXN-AS1 mitigates atherosclerosis by regulating the actin-binding protein NEXN. J Clin Invest. 2019;129(3):1115-1128. doi:10.1172/JCI98230
181. Deng S, Zhou X, Ge Z, Song Y, Wang H, Liu X, Zhang D. Exosomes from adipose-derived mesenchymal stem cells ameliorate cardiac damage after myocardial infarction by activating S1P/SK1/S1PR1 signaling and promoting macrophage M2 polarization. Int J Biochem Cell Biol. 2019;114:105564. doi:10.1016/j.biocel.2019.105564
182. Li Y, Song D, Mao L, Abraham DM, Bursac N. Lack of Thy1 defines a pathogenic fraction of cardiac fibroblasts in heart failure. Biomaterials. 2020;236:119824. doi:10.1016/j.biomaterials.2020.119824
183. Raza ST, Abbas S, Eba A, Karim F, Wani IA, Rizvi S, Zaidi A, Mahdi F. Association of COL4A1 (rs605143, rs565470) and CD14 (rs2569190) genes polymorphism with coronary artery disease. Mol Cell Biochem. 2018;445(1-2):117-122. doi:10.1007/s11010-017-3257-9
184. Azuaje F, Zhang L, Jeanty C, Puhl SL, Rodius S, Wagner DR. Analysis of a gene co-expression network establishes robust association between Col5a2 and ischemic heart disease. BMC Med Genomics. 2013;6:13. doi:10.1186/1755-8794-6-13
185. Wang X, Chen W, Zhang J, Khan A, Li L, Huang F, Qiu Z, Wang L, Chen X. Critical Role of ADAMTS2 (A Disintegrin and Metalloproteinase With Thrombospondin Motifs 2) in Cardiac Hypertrophy Induced by Pressure Overload. Hypertension. 2017;69(6):1060-1069. doi:10.1161/HYPERTENSIONAHA.116.08581
186. Hardy SA, Mabotuwana NS, Murtha LA, Coulter B, Sanchez-Bezanilla S, Al-Omary MS, Senanayake T, Loering S, Starkey M, Lee RJ, et al. Novel role of extracellular matrix protein 1 (ECM1) in cardiac aging and myocardial infarction. PLoS One. 2019;14(2):e0212230. doi:10.1371/journal.pone.0212230
187. Chen HX, Yang ZY, Hou HT, Wang J, Wang XL, Yang Q, Liu L, He GW. Novel mutations of TCTN3/LTBP2 with cellular function changes in congenital heart disease associated with polydactyly. J Cell Mol Med. 2020;24(23):13751-13762. doi:10.1111/jcmm.15950

188. El Shamieh S, Stathopoulou MG, Bonnefond A, Ndiaye NC, Lecoeur C, Meyre D, Dadé S, Chedid P, Salami A, Shahabi P, et al. Obesity status modifies the association between rs7556897T>C in the intergenic region SLC19A3-CCL20 and blood pressure in French children. Clin Chem Lab Med. 2020;58(11):1819-1827. doi:10.1515/cclm-2019-0292
189. Mastorakos G, Zapanti E. The hypothalamic-pituitary-adrenal axis in the neuroendocrine regulation of food intake and obesity: the role of corticotropin releasing hormone. Nutr Neurosci. 2004;7(5-6):271-280. doi:10.1080/10284150400020516
190. Yang H, Graham LC, Reagan AM, Grabowska WA, Schott WH, Howell GR. Transcriptome profiling of brain myeloid cells revealed activation of Itgal, Trem1, and Spp1 in western diet-induced obesity. J Neuroinflammation. 2019;16(1):169. doi:10.1186/s12974-019-1527-z
191. Du Y, Li S, Cui CJ, Zhang Y, Yang SH, Li JJ. Leptin decreases the expression of low-density lipoprotein receptor via PCSK9 pathway: linking dyslipidemia with obesity. J Transl Med. 2016;14(1):276. doi:10.1186/s12967-016-1032-4
192. Hams E, Roberts J, Bermingham R, Hogan AE, O'Shea D, O'Neill L, Fallon PG. Role for Retinoic Acid-Related Orphan Receptor Alpha (RORα) Expressing Macrophages in Diet-Induced Obesity. Front Immunol. 2020;11:1966. doi:10.3389/fimmu.2020.01966
193. Moreno-Navarrete JM, Latorre J, Lluch A, Ortega FJ, Comas F, Arnoriaga-Rodríguez M, Ricart W, Fernández-Real JM. Lysozyme is a component of the innate immune system linked to obesity associated-chronic low-grade inflammation and altered glucose tolerance. Clin Nutr. 2021;40(3):1420-1429. doi:10.1016/j.clnu.2020.08.036
194. Lee S. The association of genetically controlled CpG methylation (cg158269415) of protein tyrosine phosphatase, receptor type N2 (PTPRN2) with childhood obesity. Sci Rep. 2019;9(1):4855. doi:10.1038/s41598-019-40486-w
195. Soussi H, Reggio S, Alili R, Prado C, Mutel S, Pini M, Rouault C, Clément K, Dugail I. DAPK2 Downregulation Associates With Attenuated Adipocyte Autophagic Clearance in Human Obesity. Diabetes. 2015;64(10):3452-3463. doi:10.2337/db14-1933

196. Inoue K, Maeda N, Mori T, Sekimoto R, Tsushima Y, Matsuda K, Yamaoka M, Suganami T, Nishizawa H, Ogawa Y et al. Possible involvement of Opa-interacting protein 5 in adipose proliferation and obesity. PLoS One. 2014;9(2):e87661. doi:10.1371/journal.pone.0087661
197. Salas-Pérez F, Cuevas-Sierra A, Cuervo M, Goni L, Milagro FI, Martínez JA, Riezu-Boj JI. Differentially methylated regions (DMRs) in PON3 gene between responders and non-responders to a weight loss dietary intervention: a new tool for precision management of obesity. Epigenetics. 2021;1-12. doi:10.1080/15592294.2021.1873629
198. Lee JH, Zhang D, Kwak SE, Shin HE, Song W. Effects of Exercise and a High-Fat, High-Sucrose Restriction Diet on Metabolic Indicators, Nr4a3, and Mitochondria-Associated Protein Expression in the Gastrocnemius Muscles of Mice with Diet-Induced Obesity. J Obes Metab Syndr. 2021;10.7570/jomes20043. doi:10.7570/jomes20043
199. Han CY, Kang I, Harten IA, Gebe JA, Chan CK, Omer M, Alonge KM, den Hartigh LJ, Gomes Kjerulf D, Goodspeed L, et al. Adipocyte-Derived Versican and Macrophage-Derived Biglycan Control Adipose Tissue Inflammation in Obesity. Cell Rep. 2020;31(13):107818. doi:10.1016/j.celrep.2020.107818
200. Buchner DA, Geisinger JM, Glazebrook PA, Morgan MG, Spiezio SH, Kaiyala KJ, Schwartz MW, Sakurai T, Furley AJ, Kunze DL, et al. The juxtaparanodal proteins CNTNAP2 and TAG1 regulate diet-induced obesity. Mamm Genome. 2012;23(7-8):431-442. doi:10.1007/s00335-012-9400-8
201. Yu GI, Song DK, Shin DH. Associations of IL1RAP and IL1RL1 gene polymorphisms with obesity and inflammation mediators. Inflamm Res. 2020;69(2):191-202. doi:10.1007/s00011-019-01307-y
202. Shi Y, Long F. Hedgehog signaling via Gli2 prevents obesity induced by high-fat diet in adult mice. Elife. 2017;6:e31649. doi:10.7554/eLife.31649
203. Jo J, Sull JW, Park EJ, Jee SH. Effects of smoking and obesity on the association between CDH13 (rs3865188) and adiponectin among Korean men: the KARE study. Obesity (Silver Spring). 2012;20(8):1683-1687. doi:10.1038/oby.2011.128
204. Zhang L, Reidy SP, Nicholson TE, Lee HJ, Majdalawieh A, Webber C, Stewart BR, Dolphin P, Ro HS. The role of AEBP1 in sex-specific diet-

induced obesity. Mol Med. 2005;11(1-12):39-47. doi:10.2119/2005-00021.Ro

205. Han CY, Kang I, Harten IA, Gebe JA, Chan CK, Omer M, Alonge KM, den Hartigh LJ, Gomes Kjerulf D, Goodspeed L, et al. Adipocyte-Derived Versican and Macrophage-Derived Biglycan Control Adipose Tissue Inflammation in Obesity. Cell Rep. 2020;31(13):107818. doi:10.1016/j.celrep.2020.107818

206. Martínez-Martínez E, Rodríguez C, Galán M, Miana M, Jurado-López R, Bartolomé MV, Luaces M, Islas F, Martínez-González J, López-Andrés N, et al. The lysyl oxidase inhibitor (β-aminopropionitrile) reduces leptin profibrotic effects and ameliorates cardiovascular remodeling in diet-induced obesity in rats. J Mol Cell Cardiol. 2016;92:96-104. doi:10.1016/j.yjmcc.2016.01.012

207. Yu GI, Song DK, Shin DH. Associations of IL1RAP and IL1RL1 gene polymorphisms with obesity and inflammation mediators. Inflamm Res. 2020;69(2):191-202. doi:10.1007/s00011-019-01307-y

208. Wolff G, Taranko AE, Meln I, Weinmann J, Sijmonsma T, Lerch S, Heide D, Billeter AT, Tews D, Krunic D, et al. Diet-dependent function of the extracellular matrix proteoglycan Lumican in obesity and glucose homeostasis. Mol Metab. 2019;19:97-106. doi:10.1016/j.molmet.2018.10.007

209. Liu X, Jiang C, Yang P. Association of single nucleotide polymorphisms in the 5' upstream region of the C4BPA gene with essential hypertension in a northeastern Han Chinese population. Mol Med Rep. 2017;16(2):1289-1297. doi:10.3892/mmr.2017.6736

210. Zhang Y, Shen J, He X, Zhang K, Wu S, Xiao B, Zhou X, Phillips RS, Gao P, Jeunemaitre X, et al. A rare variant at the KYNU gene is associated with kynureninase activity and essential hypertension in the Han Chinese population. Circ Cardiovasc Genet. 2011;4(6):687-694. doi:10.1161/CIRCGENETICS.110.959064

211. Pei Q, Yang L, Tan HY, Liu SK, Liu Y, Huang L, Li RH, Wan Q, Huang J, Guo CX, et al. Effects of genetic variants in UGT1A1, SLCO1B3, ABCB1, ABCC2, ABCG2, ORM1 on PK/PD of telmisartan in Chinese patients with mild to moderate essential hypertension□. Int J Clin Pharmacol Ther. 2017;55(8):659-665. doi:10.5414/CP202744

212. Tang D, Fakiola M, Syn G, Anderson D, Cordell HJ, Scaman ESH, Davis E, Miles SJ, McLeay T, Jamieson SE, et al. Arylsulphatase A Pseudodeficiency (ARSA-PD), hypertension and chronic renal disease in Aboriginal Australians. Sci Rep. 2018;8(1):10912. doi:10.1038/s41598-018-29279-9
213. Durgin BG, Hahn SA, Schmidt HM, Miller MP, Hafeez N, Mathar I, Freitag D, Sandner P, Straub AC. Loss of smooth muscle CYB5R3 amplifies angiotensin II-induced hypertension by increasing sGC heme oxidation. JCI Insight. 2019;4(19):e129183. doi:10.1172/jci.insight.129183
214. Lai CQ, Parnell LD, Troen AM, Shen J, Caouette H, Warodomwichit D, Lee YC, Crott JW, Qiu WQ, Rosenberg IH, et al. MAT1A variants are associated with hypertension, stroke, and markers of DNA damage and are modulated by plasma vitamin B-6 and folate. Am J Clin Nutr. 2010;91(5):1377-1386. doi:10.3945/ajcn.2009.28923
215. Lipphardt M, Dihazi H, Maas JH, Schäfer AK, Amlaz SI, Ratliff BB, Koziolek MJ, Wallbach M. Syndecan-4 as a Marker of Endothelial Dysfunction in Patients with Resistant Hypertension. J Clin Med. 2020;9(9):3051. doi:10.3390/jcm9093051
216. Kho J, Tian X, Wong WT, Bertin T, Jiang MM, Chen S, Jin Z, Shchelochkov OA, Burrage LC, Reddy AK, et al. Argininosuccinate Lyase Deficiency Causes an Endothelial-Dependent Form of Hypertension. Am J Hum Genet. 2018;103(2):276-287. doi:10.1016/j.ajhg.2018.07.008
217. Yang HC, Liang YJ, Chen JW, Chiang KM, Chung CM, Ho HY, Ting CT, Lin TH, Sheu SH, Tsai WC, et al. Identification of IGF1, SLC4A4, WWOX, and SFMBT1 as hypertension susceptibility genes in Han Chinese with a genome-wide gene-based association study. PLoS One. 2012;7(3):e32907. doi:10.1371/journal.pone.0032907
218. Wu T, Zhang BQ, Raelson J, Yao YM, Wu HD, Xu ZX, Marois-Blanchet FC, Tahir MR, Wang Y, Bradley WE, et al. Analysis of the association of EPHB6, EFNB1 and EFNB3 variants with hypertension risks in males with hypogonadism. Sci Rep. 2018;8(1):14497. doi:10.1038/s41598-018-32836-x
219. Keranov S, Dörr O, Jafari L, Liebetrau C, Keller T, Troidl C, Kriechbaum S, Voss S, Richter M, Tello K, et al. SPARCL1 as a biomarker

of maladaptive right ventricular remodelling in pulmonary hypertension. Biomarkers. 2020;25(3):290-295. doi:10.1080/1354750X.2020.1745889

220. Oguri M, Kato K, Yokoi K, Watanabe S, Metoki N, Yoshida H, Satoh K, Aoyagi Y, Nishigaki Y, Yoshida H, et al. Association of polymorphisms of THBS2 and HSPA8 with hypertension in Japanese individuals with chronic kidney disease. Mol Med Rep. 2009;2(2):205-211. doi:10.3892/mmr_00000085

221. Wang Y, Hamet P, Thorin E, Tremblay J, Raelson J, Wu Z, Luo H, Jin W, Lavoie JL, Peng J, et al. Reduced blood pressure after smooth muscle EFNB2 deletion and the potential association of EFNB2 mutation with human hypertension risk. Eur J Hum Genet. 2016;24(12):1817-1825. doi:10.1038/ejhg.2016.105

222. Xu T, Shao L, Wang A, Liang R, Lin Y, Wang G, Zhao Y, Hu J, Liu S. CD248 as a novel therapeutic target in pulmonary arterial hypertension. Clin Transl Med. 2020;10(5):e175. doi:10.1002/ctm2.175

223. Cheng Q, Pan J, Zhou ZL, Yin F, Xie HY, Chen PP, Li JY, Zheng PQ, Zhou L, Zhang W, et al. Caspase-11/4 and gasdermin D-mediated pyroptosis contributes to podocyte injury in mouse diabetic nephropathy. Acta Pharmacol Sin. 2020;10.1038/s41401-020-00525-z. doi:10.1038/s41401-020-00525-z

224. Jiao X, Zhang D, Hong Q, Yan L, Han Q, Shao F, Cai G, Chen X, Zhu H. Netrin-1 works with UNC5B to regulate angiogenesis in diabetic kidney disease. Front Med. 2020;14(3):293-304. doi:10.1007/s11684-019-0715-7

225. Uehara G, Suzuki D, Toyoda M, Umezono T, Sakai H. Glomerular expression of platelet-derived growth factor (PDGF)-A, -B chain and PDGF receptor-alpha, -beta in human diabetic nephropathy. Clin Exp Nephrol. 2004;8(1):36-42. doi:10.1007/s10157-003-0265-8

226. Gregg T, Sdao SM, Dhillon RS, Rensvold JW, Lewandowski SL, Pagliarini DJ, Denu JM, Merrins MJ. Obesity-dependent CDK1 signaling stimulates mitochondrial respiration at complex I in pancreatic β-cells. J Biol Chem. 2019;294(12):4656-4666. doi:10.1074/jbc.RA118.006085

227. Fang H, Luo X, Wang Y, Liu N, Fu C, Wang H, Fang Y, Shi W, Zhang Y, Zeng C, et al. Correlation between single nucleotide polymorphisms of the ACTA2 gene and coronary artery stenosis in patients

with type 2 diabetes mellitus. Exp Ther Med. 2014;7(4):970-976. doi:10.3892/etm.2014.1510

228. Demirsoy İH, Ertural DY, Balci Ş, Çınkır Ü, Sezer K, Tamer L, Aras N. Profiles of Circulating MiRNAs Following Metformin Treatment in Patients with Type 2 Diabetes. J Med Biochem. 2018;37(4):499-506. doi:10.2478/jomb-2018-0009

229. Hourigan ST, Solly EL, Nankivell VA, Ridiandries A, Weimann BM, Henriquez R, Tepper ER, Zhang JQJ, Tsatralis T, Clayton ZE, et al. The regulation of miRNAs by reconstituted high-density lipoproteins in diabetes-impaired angiogenesis. Sci Rep. 2018;8(1):13596. doi:10.1038/s41598-018-32016-x

230. Safar HA, Chehadeh SEH, Abdel-Wareth L, Haq A, Jelinek HF, ElGhazali G, Anouti FA. Vitamin D receptor gene polymorphisms among Emirati patients with type 2 diabetes mellitus. J Steroid Biochem Mol Biol. 2018;175:119-124. doi:10.1016/j.jsbmb.2017.03.012

231. Zmuda EJ, Qi L, Zhu MX, Mirmira RG, Montminy MR, Hai T. The roles of ATF3, an adaptive-response gene, in high-fat-diet-induced diabetes and pancreatic beta-cell dysfunction. Mol Endocrinol. 2010;24(7):1423-1433. doi:10.1210/me.2009-0463

232. Boese EA, Tollefson MR, Schnieders MJ, Darbro BW, Alward WLM, Fingert JH. Novel Intragenic PAX6 Deletion in a Pedigree with Aniridia, Morbid Obesity, and Diabetes. Curr Eye Res. 2020;45(1):91-96. doi:10.1080/02713683.2019.1649704

233. Suhara T, Baba Y, Shimada BK, Higa JK, Matsui T. The mTOR Signaling Pathway in Myocardial Dysfunction in Type 2 Diabetes Mellitus. Curr Diab Rep. 2017;17(6):38. doi:10.1007/s11892-017-0865-4

234. Cabiati M, Randazzo E, Salvadori C, Peroni D, Federico G, Del Ry S. Circulating microRNAs associated with C-type natriuretic peptide in childhood obesity. Peptides. 2020;133:170387. doi:10.1016/j.peptides.2020.170387

235. Patankar JV, Chandak PG, Obrowsky S, Pfeifer T, Diwoky C, Uellen A, Sattler W, Stollberger R, Hoefler G, Heinemann A, et al. Loss of intestinal GATA4 prevents diet-induced obesity and promotes insulin sensitivity in mice. Am J Physiol Endocrinol Metab. 2011;300(3):E478-E488. doi:10.1152/ajpendo.00457.2010

236. Yan Y, Shi R, Yu X, Sun C, Zang W, Tian H. Identification of atrial fibrillation-associated microRNAs in left and right atria of rheumatic mitral valve disease patients [published correction appears in Genes Genet Syst. 2019;94(4):181]. Genes Genet Syst. 2019;94(1):23-34. doi:10.1266/ggs.17-00043
237. Ozono R. New biotechnological methods to reduce oxidative stress in the cardiovascular system: focusing on the Bach1/heme oxygenase-1 pathway. Curr Pharm Biotechnol. 2006;7(2):87-93. doi:10.2174/138920106776597630
238. Qiu C, Wang Y, Zhao H, Qin L, Shi Y, Zhu X, Song L, Zhou X, Chen J, Zhou H, et al. The critical role of SENP1-mediated GATA2 deSUMOylation in promoting endothelial activation in graft arteriosclerosis. Nat Commun. 2017;8:15426. doi:10.1038/ncomms15426
239. Liu XM, Du SL, Miao R, Wang LF, Zhong JC. Targeting the forkhead box protein P1 pathway as a novel therapeutic approach for cardiovascular diseases. Heart Fail Rev. 2020;10.1007/s10741-020-09992-2. doi:10.1007/s10741-020-09992-2
240. Fischer A, Steidl C, Wagner TU, Lang E, Jakob PM, Friedl P, Knobeloch KP, Gessler M. Combined loss of Hey1 and HeyL causes congenital heart defects because of impaired epithelial to mesenchymal transition. Circ Res. 2007;100(6):856-863. doi:10.1161/01.RES.0000260913.95642.3b
241. Hecker M, Thamilarasan M, Koczan D, Schröder I, Flechtner K, Freiesleben S, Füllen G, Thiesen HJ, Zettl UK. MicroRNA expression changes during interferon-beta treatment in the peripheral blood of multiple sclerosis patients. Int J Mol Sci. 2013;14(8):16087-16110.. doi:10.3390/ijms140816087
242. Gu X, Liu Y, Wang N, Zhen J, Zhang B, Hou S, Cui Z, Wan Q, Feng H. Transcription of MRPL12 regulated by Nrf2 contributes to the mitochondrial dysfunction in diabetic kidney disease. Free Radic Biol Med. 2021;164:329-340. doi:10.1016/j.freeradbiomed.2021.01.004
243. Zhang D, Gu T, Forsberg E, Efendic S, Brismar K, Gu HF. Genetic and functional effects of membrane metalloendopeptidase on diabetic nephropathy development. Am J Nephrol. 2011;34(5):483-490. doi:10.1159/000333006

244. Bourgeois A, Bonnet S, Breuils-Bonnet S, Habbout K, Paradis R, Tremblay E, Lampron MC, Orcholski ME, Potus F, Bertero T, et al. Inhibition of CHK 1 (Checkpoint Kinase 1) Elicits Therapeutic Effects in Pulmonary Arterial Hypertension. Arterioscler Thromb Vasc Biol. 2019;39(8):1667-1681. doi:10.1161/ATVBAHA.119.312537

Tables

Table 1 The sequences of primers for quantitative RT-PCR

Genes	Forward Primers	Reverse Primers
JUN	TTCCTCCAGTCCGAGAGCG	TGAGAAGGTCCGAGTTCTTGG
VCAM1	TTGGGAGCCTCAACGGTACT	GCAATCGTTTTGTATTCAGGGGA
RELA	TGCGATTCCGCTATAAATGCG	ACAAGTTCATGTGGATGAGGC
U2AF2	ATGTCGGACTTCGACGAGTTC	CCTGTGCCGATTCTCCTTGT
ADRB2	ATGTCGGTTATCGTCCTGGC	GGTTTGTAGTCGCTCGAACTTG
FN1	ATGTGGACCCCTCCTGATAGT	GCCCAGTGATTTCAGCAAAGG
CDK1	AGGTACTTACGGTGTGGTGTAT	CTCGCTTTCAAGTCTGATCTTCT
TK1	AGTGCCTGGTCATCAAGTATGC	GCTGCCACAATTACTGTCTTGC
A2M	GGCAGAATTTCCGCTTAGAGG	CACACACGGACACATTCATCT
ACTA2	CCCAGACATCAGGGAGTAATGG	TCTATCGGATACTTCAGCGTCA

Table 2 The statistical metrics for key differentially expressed genes (DEGs)

Gene Symbol	logFC	pValue	adj.P.Val	tvalue	Regulation	Gene Name
PENK	4.860097	2.31E-06	6.52E-05	4.724639	Up	proenkephalin
CYP4F11	4.557396	1.08E-08	6.35E-07	5.718164	Up	cytochrome P450 family 4 subfamily F member 11
SAA1	4.462926	1.67E-10	1.47E-08	6.389109	Up	serum amyloid A1
CARTPT	4.198389	4.41E-06	0.000113	4.591213	Up	CART prepropeptide
SUCNR1	4.145076	1.59E-08	8.96E-07	5.651175	Up	succinate receptor 1
ORM1	3.813821	8.85E-06	0.000205	4.443579	Up	orosomucoid 1
CRP	3.755592	3.74E-42	3.70E-39	13.60499	Up	C-reactive protein
ITGAX	3.641001	2.84E-06	7.77E-05	4.681713	Up	integrin subunit alpha X
APCS	3.628065	6.73E-19	2.00E-16	8.87927	Up	amyloid P component, serum
CA12	3.545671	6.04E-13	8.54E-11	7.199606	Up	carbonic anhydrase 12
CACNA2D3	3.499413	2.91E-07	1.12E-05	5.128975	Up	calcium voltage-gated channel auxiliary subunit alpha2delta 3
SLITRK6	3.470335	1.29E-14	2.33E-12	7.706578	Up	SLIT and NTRK like family member 6

F11	3.438039	1.28E-11	1.45E-09	6.771333	Up	coagulation factor XI
CHI3L2	3.353492	0.003527	0.025134	2.917594	Up	chitinase 3 like 2
MUC15	3.285	5.44E-05	0.000915	4.035669	Up	mucin 15, cell surface associated
MSMB	3.271431	0.007069	0.041925	2.693557	Up	microseminoprotein beta
UCA1	3.175529	4.97E-12	6.20E-10	6.906567	Up	urothelial cancer associated 1
C4BPA	3.156304	7.62E-08	3.42E-06	5.375891	Up	complement component 4 binding protein alpha
SERPINA6	3.094247	1.58E-14	2.79E-12	7.680819	Up	serpin family A member 6
FGFBP1	3.063736	5.24E-05	0.000889	4.044509	Up	fibroblast growth factor binding protein 1
FGA	3.039962	2.40E-05	0.000469	4.224153	Up	fibrinogen alpha chain
HAO1	2.988341	0.008352	0.047393	2.6375	Up	hydroxyacid oxidase 1
PIGR	2.974332	3.80E-22	1.48E-19	9.676431	Up	polymeric immunoglobulin receptor
PPY	2.954157	6.32E-32	3.61E-29	11.75944	Up	pancreatic polypeptide
ALDH1A2	2.942058	0.000702	0.00735	3.38886	Up	aldehyde dehydrogenase 1 family member A2
PSTPIP2	2.936601	0.000134	0.001922	3.81981	Up	proline-serine-threonine phosphatase interacting protein 2
SAA2	2.886413	0.000194	0.002625	3.726124	Up	serum amyloid A2
SNORA62	2.866455	0.000796	0.008139	3.354352	Up	small nucleolar RNA, H/ACA box 62
LRG1	2.815781	3.99E-09	2.54E-07	5.884742	Up	leucine rich alpha-2-glycoprotein 1
C16orf54	2.814328	0.000711	0.00743	3.385114	Up	chromosome 16 open reading frame 54
RGS1	2.76984	0.000395	0.004659	3.543409	Up	regulator of G protein signaling 1
TMEM132B	2.721191	3.82E-09	2.44E-07	5.891843	Up	transmembrane protein 132B
AMBN	2.717325	0.005864	0.036494	2.75531	Up	ameloblastin
STX19	2.699996	1.05E-05	0.000235	4.407223	Up	syntaxin 19
RAB33A	2.694358	0.006201	0.038131	2.736957	Up	RAB33A, member RAS oncogene family
KYNU	2.63086	0.000374	0.004463	3.557871	Up	kynureninase
LOC389834	2.602019	1.62E-11	1.79E-09	6.736442	Up	ankyrin repeat domain 57 pseudogene
SLC17A1	2.594486	0.003475	0.024908	2.922231	Up	solute carrier family 17 member 1
ADRB2	2.548793	0.001254	0.011599	3.226378	Up	adrenoceptor beta 2
AADAC	2.519181	0.004121	0.028255	2.868728	Up	arylacetamide deacetylase
VNN1	2.51097	4.17E-09	2.65E-07	5.877277	Up	vanin 1
SLPI	2.505407	9.85E-11	9.02E-09	6.469308	Up	secretory leukocyte peptidase inhibitor
SLCO1A2	2.502753	0.000923	0.009176	3.313154	Up	solute carrier organic anion transporter family member 1A2
ST8SIA1	2.488529	2.41E-06	6.74E-05	4.715297	Up	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 1
NRAP	2.399155	4.27E-05	0.000748	4.092199	Up	nebulin related anchoring protein
HLA-DRA	2.388682	2.35E-08	1.25E-06	5.584286	Up	major histocompatibility complex, class II, DR alpha
CHI3L1	2.387761	2.28E-06	6.49E-05	4.72652	Up	chitinase 3 like 1
SLC19A3	2.385339	0.001489	0.013224	3.176838	Up	solute carrier family 19 member 3
AMBP	2.361932	1.13E-11	1.30E-09	6.788459	Up	alpha-1-microglobulin/bikunin precursor
REG3A	2.360754	1.23E-16	2.77E-14	8.279959	Up	regenerating family member 3 alpha
SLITRK1	2.357923	0.000111	0.001645	3.864203	Up	SLIT and NTRK like family member 1
IDUA	2.326669	4.20E-06	0.000109	4.601026	Up	alpha-L-iduronidase
GLB1L3	2.31374	0.00073	0.007589	3.377954	Up	galactosidase beta 1 like 3
CCL20	2.287171	1.33E-06	4.22E-05	4.834695	Up	C-C motif chemokine ligand 20
VNN2	2.286735	7.10E-06	0.000169	4.490666	Up	vanin 2

LOC100287042	2.281235	3.41E-05	0.000622	4.144375	Up	uncharacterized LOC100287042
SLC25A19	2.270193	2.32E-06	6.56E-05	4.723098	Up	solute carrier family 25 member 19
GABRE	2.249575	0.002005	0.016626	3.089455	Up	gamma-aminobutyric acid type A receptor subunit epsilon
NR1H4	2.247257	0.001413	0.012715	3.192038	Up	nuclear receptor subfamily 1 group H member 4
TSPAN8	2.233034	1.85E-12	2.50E-10	7.045428	Up	tetraspanin 8
CEACAM7	2.226633	5.58E-08	2.64E-06	5.43174	Up	CEA cell adhesion molecule 7
CA4	2.191782	0.006301	0.038587	2.731677	Up	carbonic anhydrase 4
CERS1	2.18001	0.006481	0.039298	2.722409	Up	ceramide synthase 1
CDH17	2.177532	0.002096	0.017108	3.076347	Up	cadherin 17
PPP1R1B	2.15086	0.00586	0.036487	2.755516	Up	protein phosphatase 1 regulatory inhibitor subunit 1B
ACSF3	2.095319	0.000462	0.005303	3.501601	Up	acyl-CoA synthetase family member 3
FFAR1	2.080867	0.005375	0.03423	2.783637	Up	free fatty acid receptor 1
SERPINA10	2.046459	8.11E-06	0.00019	4.462269	Up	serpin family A member 10
FIGNL1	2.041234	4.60E-05	0.000794	4.07531	Up	fidgetin like 1
ADH1C	2.037037	4.35E-06	0.000112	4.594134	Up	alcohol dehydrogenase 1C (class I), gamma polypeptide
HLA-DMB	2.032997	0.005544	0.035075	2.773628	Up	major histocompatibility complex, class II, DM beta
SLC34A2	2.032368	2.84E-05	0.00054	4.186165	Up	solute carrier family 34 member 2
SPATA2L	2.020068	5.03E-05	0.00086	4.054045	Up	spermatogenesis associated 2 like
HCN3	1.997149	5.93E-08	2.76E-06	5.420837	Up	hyperpolarization activated cyclic nucleotide gated potassium channel 3
KCTD16	1.962394	0.003351	0.024334	2.933559	Up	potassium channel tetramerization domain containing 16
PKLR	1.928837	3.46E-06	9.23E-05	4.641383	Up	pyruvate kinase L/R
DUOXA2	1.924972	1.06E-06	3.44E-05	4.880573	Up	dual oxidase maturation factor 2
FA2H	1.92455	0.002863	0.021636	2.982087	Up	fatty acid 2-hydroxylase
TUB	1.917857	1.09E-07	4.74E-06	5.311478	Up	TUB bipartite transcription factor
PID1	1.916368	0.004177	0.028518	2.864483	Up	phosphotyrosine interaction domain containing 1
MLIP	1.913434	2.16E-07	8.57E-06	5.184749	Up	muscular LMNA interacting protein
GCNT3	1.908059	1.93E-08	1.06E-06	5.618207	Up	glucosaminyl (N-acetyl) transferase 3, mucin type
OTOGL	1.892097	1.00E-04	0.001501	3.890689	Up	otogelin like
CDKN2A	1.883974	0.00094	0.009327	3.307815	Up	cyclin dependent kinase inhibitor 2A
MACROD1	1.872259	0.007006	0.04162	2.696554	Up	mono-ADP ribosylhydrolase 1
VCAM1	1.871446	3.76E-06	9.91E-05	4.624033	Up	vascular cell adhesion molecule 1
LGALS4	1.84876	9.70E-06	0.00022	4.423816	Up	galectin 4
TMEM143	1.846802	0.001428	0.012824	3.188908	Up	transmembrane protein 143
CRH	1.827098	2.35E-06	6.62E-05	4.720469	Up	corticotropin releasing hormone
WDR72	1.824566	0.008691	0.048752	2.623982	Up	WD repeat domain 72
WDR24	1.819369	0.001795	0.015187	3.122228	Up	WD repeat domain 24
KCNQ1	1.817087	1.48E-05	0.000311	4.331946	Up	potassium voltage-gated channel subfamily Q member 1
NR4A2	1.815373	1.42E-10	1.27E-08	6.413344	Up	nuclear receptor subfamily 4 group A member 2
NECAB2	1.813422	0.001222	0.011371	3.233672	Up	N-terminal EF-hand calcium binding protein 2
URB2	1.811519	8.32E-05	0.001288	3.93486	Up	URB2 ribosome biogenesis homolog
ALB	1.794782	1.48E-05	0.000311	4.331897	Up	albumin
KCNH6	1.77235	5.47E-05	0.000915	4.03459	Up	potassium voltage-gated channel subfamily H member 6
CNGA1	1.769682	5.46E-05	0.000915	4.035139	Up	cyclic nucleotide gated channel subunit alpha 1

MAT1A	1.766294	0.00023	0.003021	3.683726	Up	methionine adenosyltransferase 1A
SLC24A3	1.759392	0.004454	0.029889	2.844072	Up	solute carrier family 24 member 3
DAB2IP	1.759192	7.46E-07	2.52E-05	4.949072	Up	DAB2 interacting protein
SNORA20	1.756052	0.003502	0.025024	2.919876	Up	small nucleolar RNA, H/ACA box 20
ARRDC2	1.750189	6.94E-06	0.000166	4.495401	Up	arrestin domain containing 2
PLIN5	1.739472	0.006153	0.037942	2.739541	Up	perilipin 5
SLC6A20	1.736959	0.008503	0.047957	2.631413	Up	solute carrier family 6 member 20
CD74	1.736016	2.32E-11	2.48E-09	6.684348	Up	CD74 molecule
DUOXA1	1.726737	5.87E-05	0.000971	4.018021	Up	dual oxidase maturation factor 1
CP	1.7227	2.93E-10	2.44E-08	6.302509	Up	ceruloplasmin
ALDOB	1.721723	0.000101	0.001509	3.889197	Up	aldolase, fructose-bisphosphate B
OIP5	1.717334	0.008267	0.047125	2.640977	Up	Opa interacting protein 5
HLA-F-AS1	1.716992	4.92E-06	0.000124	4.568213	Up	HLA-F antisense RNA 1
PCDH10	1.715746	0.001468	0.01308	3.18087	Up	protocadherin 10
FJX1	1.693333	0.003956	0.027372	2.881683	Up	four-jointed box kinase 1
MAP3K9	1.683732	9.32E-06	0.000214	4.432432	Up	mitogen-activated protein kinase kinase kinase 9
HABP2	1.681662	0.000412	0.004825	3.532477	Up	hyaluronan binding protein 2
BRD7P3	1.677208	0.000205	0.002741	3.712458	Up	bromodomain containing 7 pseudogene 3
SHROOM1	1.671713	1.55E-08	8.74E-07	5.656164	Up	shroom family member 1
PTPRH	1.669188	0.000118	0.001725	3.85006	Up	protein tyrosine phosphatase receptor type H
SHANK2	1.665031	0.000579	0.006326	3.441284	Up	SH3 and multiple ankyrin repeat domains 2
PGR	1.657716	1.99E-09	1.33E-07	5.999007	Up	progesterone receptor
PHLDA3	1.65533	0.000794	0.008137	3.354941	Up	pleckstrin homology like domain family A member 3
S100Z	1.652261	0.00568	0.035738	2.765729	Up	S100 calcium binding protein Z
SOCS1	1.634331	0.003513	0.025042	2.918905	Up	suppressor of cytokine signaling 1
ASPSCR1	1.624667	0.000167	0.002316	3.764994	Up	ASPSCR1 tether for SLC2A4, UBX domain containing
BIRC3	1.618173	5.91E-09	3.66E-07	5.819157	Up	baculoviral IAP repeat containing 3
C1QTNF4	1.614263	0.004843	0.031685	2.817264	Up	C1q and TNF related 4
RNF32	1.601341	0.005621	0.035412	2.76913	Up	ring finger protein 32
VARS2	1.58278	0.000596	0.006463	3.433317	Up	valyl-tRNA synthetase 2, mitochondrial
PLEKHB1	1.578123	5.54E-05	0.000926	4.031511	Up	pleckstrin homology domain containing B1
CDH22	1.571917	0.005098	0.03286	2.800754	Up	cadherin 22
DOCK8	1.567052	0.004065	0.027932	2.873092	Up	dedicator of cytokinesis 8
SERTM1	1.564759	0.001697	0.014507	3.13872	Up	serine rich and transmembrane domain containing 1
ADRB1	1.554144	0.001395	0.012583	3.195745	Up	adrenoceptor beta 1
CALY	1.543282	0.000114	0.001673	3.858656	Up	calcyon neuron specific vesicular protein
ACSS2	1.542	7.54E-05	0.001186	3.958622	Up	acyl-CoA synthetase short chain family member 2
JMJD4	1.540229	0.000174	0.002405	3.754382	Up	jumonji domain containing 4
STEAP4	1.533888	0.004097	0.028125	2.870632	Up	STEAP4 metalloreductase
OSGIN2	1.529591	1.60E-06	4.91E-05	4.798679	Up	oxidative stress induced growth inhibitor family member 2
SPP1	1.527485	4.18E-11	4.25E-09	6.597665	Up	secreted phosphoprotein 1
ZNF784	1.523025	0.008388	0.047542	2.636046	Up	zinc finger protein 784
RHOT2	1.510241	1.68E-08	9.37E-07	5.642248	Up	ras homolog family member T2

DPP4	1.507531	1.17E-06	3.76E-05	4.860897	Up	dipeptidyl peptidase 4
DEFB1	1.505726	5.22E-05	0.000885	4.045675	Up	defensin beta 1
FAM20A	1.500559	0.005505	0.034873	2.775919	Up	FAM20A golgi associated secretory pathway pseudokinase
KLB	1.489726	0.001201	0.011223	3.238649	Up	klotho beta
CLIP2	1.487029	0.000132	0.001905	3.823121	Up	CAP-Gly domain containing linker protein 2
MVD	1.483339	0.000281	0.003571	3.631897	Up	mevalonate diphosphate decarboxylase
SCNN1A	1.482171	0.005552	0.035114	2.773124	Up	sodium channel epithelial 1 subunit alpha
LRRC24	1.468999	0.000285	0.003597	3.628672	Up	leucine rich repeat containing 24
ELL	1.459712	0.002701	0.020786	2.999815	Up	elongation factor for RNA polymerase II
CCDC85B	1.454035	0.000695	0.007327	3.391678	Up	coiled-coil domain containing 85B
DENND2D	1.448171	2.07E-06	6.02E-05	4.746846	Up	DENN domain containing 2D
NR4A3	1.443348	0.000701	0.00735	3.389062	Up	nuclear receptor subfamily 4 group A member 3
PEX7	1.441084	0.000698	0.00735	3.39031	Up	peroxisomal biogenesis factor 7
CASP10	1.43516	0.001067	0.010216	3.272233	Up	caspase 10
RNASE4	1.434292	8.21E-09	4.96E-07	5.764056	Up	ribonuclease A family member 4
GGA1	1.422219	2.17E-06	6.27E-05	4.736599	Up	golgi associated, gamma adaptin ear containing, ARF binding protein 1
ZBTB48	1.420898	5.67E-06	0.00014	4.538176	Up	zinc finger and BTB domain containing 48
ARX	1.41982	4.88E-07	1.75E-05	5.031034	Up	aristaless related homeobox
HLA-DRB1	1.417078	0.005289	0.033753	2.788877	Up	major histocompatibility complex, class II, DR beta 1
HSD17B2	1.41604	0.005122	0.032969	2.799273	Up	hydroxysteroid 17-beta dehydrogenase 2
FAM98C	1.412537	0.001652	0.014229	3.146501	Up	family with sequence similarity 98 member C
KLKB1	1.408861	0.003203	0.023502	2.94759	Up	kallikrein B1
KLHDC1	1.40424	0.000949	0.009368	3.305269	Up	kelch domain containing 1
RAB20	1.402783	0.007176	0.042473	2.688558	Up	RAB20, member RAS oncogene family
DUOX2	1.400604	8.92E-06	0.000206	4.441768	Up	dual oxidase 2
CASP1	1.396972	0.004561	0.030411	2.836529	Up	caspase 1
CHN2	1.393794	0.00846	0.047791	2.633124	Up	chimerin 2
KCNC4	1.383783	0.001837	0.015486	3.115314	Up	potassium voltage-gated channel subfamily C member 4
ARMC7	1.382084	3.64E-05	0.000655	4.128939	Up	armadillo repeat containing 7
LAT2	1.375052	0.008875	0.049473	2.616818	Up	linker for activation of T cells family member 2
WFDC2	1.361957	4.56E-05	0.000788	4.077326	Up	WAP four-disulfide core domain 2
NPAS4	1.357653	0.002985	0.022333	2.969242	Up	neuronal PAS domain protein 4
HLA-DPB1	1.353913	0.008542	0.048154	2.629871	Up	major histocompatibility complex, class II, DP beta 1
RARRES2	1.349155	0.002552	0.019943	3.017143	Up	retinoic acid receptor responder 2
RFX1	1.349082	7.70E-05	0.001207	3.953595	Up	regulatory factor X1
CYP3A5	1.33808	2.89E-06	7.86E-05	4.67874	Up	cytochrome P450 family 3 subfamily A member 5
MIR29C	1.334143	0.000797	0.008139	3.353784	Up	microRNA 29c
MRPL12	1.333729	0.001991	0.016546	3.091565	Up	mitochondrial ribosomal protein L12
FBXO36	1.333024	1.23E-05	0.000269	4.372934	Up	F-box protein 36
FAM86DP	1.328847	0.005607	0.035369	2.76994	Up	family with sequence similarity 86 member D, pseudogene
ARVCF	1.326161	3.31E-05	0.00061	4.150713	Up	ARVCF delta catenin family member
DEPTOR	1.318149	0.001117	0.010593	3.259253	Up	DEP domain containing MTOR interacting protein
KCNJ8	1.318057	0.000238	0.003115	3.674944	Up	potassium inwardly rectifying channel subfamily J member 8

PDZK1IP1	1.315801	9.18E-05	0.001398	3.911373	Up	PDZK1 interacting protein 1
CFB	1.315099	3.82E-06	9.99E-05	4.621177	Up	complement factor B
CPT1B	1.308267	0.000694	0.007327	3.391758	Up	carnitine palmitoyltransferase 1B
MMRN1	1.306941	0.000963	0.009463	3.30117	Up	multimerin 1
ETV3	1.301854	0.001294	0.011913	3.217317	Up	ETS variant transcription factor 3
DTNB	1.283314	0.005856	0.036476	2.755748	Up	dystrobrevin beta
MMP1	1.282851	0.000374	0.004463	3.557922	Up	matrix metallopeptidase 1
TMEM176A	1.282033	6.86E-10	5.17E-08	6.169302	Up	transmembrane protein 176A
NR4A1	1.277418	9.03E-10	6.61E-08	6.125627	Up	nuclear receptor subfamily 4 group A member 1
TYMP	1.269805	0.003887	0.02702	2.887229	Up	thymidine phosphorylase
WHAMMP3	1.268427	0.00011	0.001633	3.86674	Up	WAS protein homolog associated with actin, golgi membranes and microtubules pseudogene 3
GPX2	1.266532	1.24E-06	3.98E-05	4.848674	Up	glutathione peroxidase 2
MRC1	1.265704	0.002608	0.020311	3.010482	Up	mannose receptor C-type 1
SLC28A3	1.261081	0.005242	0.033569	2.791764	Up	solute carrier family 28 member 3
GRINA	1.260001	1.66E-09	1.13E-07	6.028311	Up	glutamate ionotropic receptor NMDA type subunit associated protein 1
COMTD1	1.259376	0.000438	0.005062	3.516212	Up	catechol-O-methyltransferase domain containing 1
ITPKC	1.253391	0.003493	0.025012	2.92061	Up	inositol-trisphosphate 3-kinase C
LTBP3	1.251497	8.68E-07	2.89E-05	4.919326	Up	latent transforming growth factor beta binding protein 3
MT1A	1.250232	0.001512	0.013377	3.172284	Up	metallothionein 1A
ZNF34	1.239207	0.001255	0.011605	3.226068	Up	zinc finger protein 34
FBXW5	1.233028	1.30E-06	4.11E-05	4.840395	Up	F-box and WD repeat domain containing 5
LCN2	1.224204	1.29E-05	0.00028	4.362318	Up	lipocalin 2
CEACAM19	1.214525	0.007367	0.04329	2.679795	Up	CEA cell adhesion molecule 19
PRLR	1.214388	0.002876	0.021699	2.980724	Up	prolactin receptor
ZNF862	1.210155	0.003181	0.023371	2.949721	Up	zinc finger protein 862
STXBP6	1.205294	0.000536	0.00594	3.462271	Up	syntaxin binding protein 6
DUSP8	1.202609	8.43E-05	0.001299	3.931698	Up	dual specificity phosphatase 8
ZC3H12A	1.195651	0.001091	0.010383	3.265831	Up	zinc finger CCCH-type containing 12A
LHPP	1.194241	0.003948	0.027329	2.882321	Up	phospholysine phosphohistidine inorganic pyrophosphate phosphatase
GP2	1.191415	0.002309	0.018474	3.047314	Up	glycoprotein 2
SIK1	1.18886	1.21E-05	0.000266	4.376562	Up	salt inducible kinase 1
SERPING1	1.188811	1.08E-05	0.00024	4.401319	Up	serpin family G member 1
ATP13A2	1.188695	0.003061	0.022786	2.961525	Up	ATPase cation transporting 13A2
ADORA2A	1.188079	0.002256	0.018136	3.054326	Up	adenosine A2a receptor
BTG2	1.187414	2.04E-12	2.70E-10	7.031727	Up	BTG anti-proliferation factor 2
SEMA3E	1.184185	2.70E-05	0.000518	4.197493	Up	semaphorin 3E
MUC13	1.181307	2.25E-07	8.87E-06	5.177146	Up	mucin 13, cell surface associated
STS	1.181228	0.007185	0.042494	2.688133	Up	steroid sulfatase
CPM	1.180739	0.000637	0.006829	3.415186	Up	carboxypeptidase M
PPP1R12B	1.178311	0.00055	0.006085	3.45499	Up	protein phosphatase 1 regulatory subunit 12B
TMEM30B	1.174283	6.10E-08	2.81E-06	5.415896	Up	transmembrane protein 30B
UNC119B	1.172844	0.000104	0.00155	3.880943	Up	unc-119 lipid binding chaperone B

CHRNE	1.172479	0.000127	0.001847	3.831284	Up	cholinergic receptor nicotinic epsilon subunit
RPS6KA6	1.170868	0.000293	0.003668	3.621693	Up	ribosomal protein S6 kinase A6
ITGB3BP	1.16542	2.55E-05	0.000496	4.210131	Up	integrin subunit beta 3 binding protein
TPSG1	1.160373	0.001307	0.011969	3.214515	Up	tryptase gamma 1
TNFAIP2	1.159342	3.35E-05	0.000615	4.14848	Up	TNF alpha induced protein 2
ZBTB7A	1.155527	9.88E-10	7.16E-08	6.111375	Up	zinc finger and BTB domain containing 7A
BBC3	1.154274	0.006236	0.03831	2.735096	Up	BCL2 binding component 3
EPS8L2	1.149059	2.71E-06	7.46E-05	4.691359	Up	EPS8 like 2
DAPK2	1.148499	0.00055	0.006084	3.455243	Up	death associated protein kinase 2
SDC4	1.147833	2.13E-06	6.17E-05	4.740494	Up	syndecan 4
SPOCK3	1.147027	0.001613	0.013975	3.153535	Up	SPARC (osteonectin), cwcv and kazal like domains proteoglycan 3
ZFP36	1.145497	4.76E-10	3.82E-08	6.226781	Up	ZFP36 ring finger protein
CA2	1.144512	0.003937	0.02728	2.883181	Up	carbonic anhydrase 2
GRAMD4	1.143431	0.000704	0.007369	3.38796	Up	GRAM domain containing 4
KIFC2	1.137498	0.006227	0.038275	2.735575	Up	kinesin family member C2
RASSF5	1.136232	2.75E-06	7.55E-05	4.688523	Up	Ras association domain family member 5
CTSD	1.132154	3.47E-11	3.60E-09	6.625256	Up	cathepsin D
SPTSSB	1.131418	0.000381	0.004523	3.553075	Up	serine palmitoyltransferase small subunit B
SOD2	1.126412	6.27E-11	6.21E-09	6.537195	Up	superoxide dismutase 2
ROGDI	1.125008	0.000108	0.001606	3.871842	Up	rogdi atypical leucine zipper
WHAMMP2	1.122241	0.001637	0.014145	3.149165	Up	WAS protein homolog associated with actin, golgi membranes and microtubules pseudogene 2
JAKMIP1	1.121972	0.007586	0.044265	2.669952	Up	janus kinase and microtubule interacting protein 1
SMOC1	1.120388	4.12E-05	0.000724	4.100379	Up	SPARC related modular calcium binding 1
KAT8	1.118592	0.000671	0.00712	3.401263	Up	lysine acetyltransferase 8
MRS2P2	1.109493	0.005082	0.032798	2.801787	Up	MRS2 pseudogene 2
PBX2	1.106311	0.000883	0.008875	3.325261	Up	PBX homeobox 2
NAT9	1.105312	0.00236	0.018801	3.040739	Up	N-acetyltransferase 9 (putative)
GBP2	1.097352	0.00316	0.023257	2.951688	Up	guanylate binding protein 2
APOH	1.0953	0.001207	0.01127	3.237117	Up	apolipoprotein H
ARSA	1.094952	8.14E-05	0.001267	3.940246	Up	arylsulfatase A
PIM3	1.093568	6.09E-05	0.000997	4.009468	Up	Pim-3 proto-oncogene, serine/threonine kinase
DDX25	1.087549	0.008743	0.048956	2.621949	Up	DEAD-box helicase 25
EGR3	1.083482	0.004081	0.02803	2.871842	Up	early growth response 3
RAB17	1.080047	0.000476	0.00542	3.493738	Up	RAB17, member RAS oncogene family
SNORD102	1.078771	0.000943	0.009353	3.306857	Up	small nucleolar RNA, C/D box 102
GSDMD	1.07772	0.001234	0.011455	3.230845	Up	gasdermin D
HLA-B	1.072221	2.50E-17	6.18E-15	8.467954	Up	major histocompatibility complex, class I, B
PON3	1.071857	0.00437	0.029495	2.850165	Up	paraoxonase 3
C1R	1.071156	0.003238	0.023686	2.944197	Up	complement C1r
HYI	1.069764	4.05E-05	0.000713	4.104388	Up	hydroxypyruvate isomerase (putative)
DDX54	1.068929	0.001651	0.014228	3.146782	Up	DEAD-box helicase 54
LONP1	1.066421	9.16E-06	0.000211	4.436098	Up	lon peptidase 1, mitochondrial

SERPINA1	1.062074	1.98E-08	1.08E-06	5.614097	Up	serpin family A member 1
MGC70870	1.055503	0.004001	0.027598	2.878076	Up	C-terminal binding protein 2 pseudogene
UBD	1.054856	0.007211	0.042594	2.686948	Up	ubiquitin D
CASZ1	1.054643	0.003332	0.024209	2.935302	Up	castor zinc finger 1
SNCA	1.052071	0.001465	0.013067	3.181438	Up	synuclein alpha
ONECUT2	1.050612	0.000491	0.005529	3.485354	Up	one cut homeobox 2
EGR4	1.047477	0.003331	0.024209	2.935462	Up	early growth response 4
PNLIP	1.044398	0.001947	0.01625	3.098235	Up	pancreatic lipase
SLC29A4	1.044248	8.53E-05	0.001311	3.928868	Up	solute carrier family 29 member 4
JUN	1.041042	5.35E-11	5.37E-09	6.560931	Up	Jun proto-oncogene, AP-1 transcription factor subunit
OCRL	1.035964	0.000137	0.001962	3.813522	Up	OCRL inositol polyphosphate-5-phosphatase
DHCR24	1.031289	3.93E-05	0.000696	4.111443	Up	24-dehydrocholesterol reductase
TMC5	1.028393	0.001332	0.012139	3.209069	Up	transmembrane channel like 5
FSTL5	1.022268	0.000867	0.008745	3.330316	Up	follistatin like 5
RAP1A	1.013348	2.63E-06	7.26E-05	4.698065	Up	RAP1A, member of RAS oncogene family
AOX1	1.012166	0.002812	0.021393	2.987574	Up	aldehyde oxidase 1
ZNF692	1.011426	0.002003	0.01662	3.089814	Up	zinc finger protein 692
SLC22A17	1.011289	3.88E-07	1.44E-05	5.074865	Up	solute carrier family 22 member 17
TRAPPC5	1.010652	5.56E-07	1.94E-05	5.005747	Up	trafficking protein particle complex 5
CTSS	1.010378	0.000557	0.006137	3.451709	Up	cathepsin S
COX5A	1.008381	2.21E-11	2.37E-09	6.691712	Up	cytochrome c oxidase subunit 5A
NUDT16	1.004815	0.002233	0.01798	3.057404	Up	nudix hydrolase 16
C1orf122	0.998501	1.80E-06	5.45E-05	4.774514	Up	chromosome 1 open reading frame 122
SNHG1	0.992947	0.001731	0.014763	3.132913	Up	small nucleolar RNA host gene 1
ABHD12	0.98966	4.40E-05	0.000766	4.08564	Up	abhydrolase domain containing 12, lysophospholipase
MIR147B	0.989371	1.01E-06	3.31E-05	4.889678	Up	microRNA 147b
TTR	0.98906	2.80E-11	2.95E-09	6.656749	Up	transthyretin
RAB27A	0.986412	0.000326	0.004015	3.593435	Up	RAB27A, member RAS oncogene family
GNAI1	0.98537	5.81E-07	2.02E-05	4.997344	Up	G protein subunit alpha i1
TM4SF4	0.982872	1.68E-08	9.37E-07	5.642406	Up	transmembrane 4 L six family member 4
SCN3A	0.981372	0.001031	0.009986	3.281956	Up	sodium voltage-gated channel alpha subunit 3
TMED10P1	0.981285	1.17E-09	8.18E-08	6.084545	Up	transmembrane p24 trafficking protein 10 pseudogene 1
SLC16A7	0.979185	0.003043	0.022676	2.963325	Up	solute carrier family 16 member 7
IL6R	0.97521	0.002568	0.020043	3.01516	Up	interleukin 6 receptor
IMPA2	0.974629	0.004064	0.027932	2.873126	Up	inositol monophosphatase 2
DUSP1	0.97403	1.62E-09	1.11E-07	6.032277	Up	dual specificity phosphatase 1
HSPA1B	0.973353	1.57E-06	4.84E-05	4.802269	Up	heat shock protein family A (Hsp70) member 1B
SLC12A7	0.970748	0.000457	0.005244	3.504999	Up	solute carrier family 12 member 7
NAGLU	0.967873	0.001187	0.011106	3.242006	Up	N-acetyl-alpha-glucosaminidase
DLEC1	0.95751	0.001453	0.012998	3.183982	Up	DLEC1 cilia and flagella associated protein
C15orf48	0.957485	1.05E-07	4.62E-06	5.317105	Up	chromosome 15 open reading frame 48
ABCB1	0.951745	0.000274	0.003499	3.638721	Up	ATP binding cassette subfamily B member 1
RIPPLY2	0.949701	0.003964	0.027394	2.880986	Up	ripply transcriptional repressor 2

XAB2	0.947952	0.004995	0.032378	2.80736	Up	XPA binding protein 2
PTP4A1	0.944972	3.71E-12	4.71E-10	6.947816	Up	protein tyrosine phosphatase 4A1
GBA2	0.942585	0.000161	0.002251	3.774149	Up	glucosylceramidase beta 2
F10	0.941789	0.000946	0.009363	3.305991	Up	coagulation factor X
ANG	0.940414	0.000569	0.006246	3.445744	Up	angiogenin
AFMID	0.940065	0.000663	0.007049	3.404575	Up	arylformamidase
ASL	0.939426	0.000486	0.005494	3.488568	Up	argininosuccinate lyase
POLD3	0.937297	0.001543	0.013561	3.166421	Up	DNA polymerase delta 3, accessory subunit
SERTAD3	0.932907	0.004437	0.029803	2.845289	Up	SERTA domain containing 3
GABBR1	0.93278	0.008879	0.049473	2.616667	Up	gamma-aminobutyric acid type B receptor subunit 1
CACNA1H	0.924741	0.008616	0.048407	2.626944	Up	calcium voltage-gated channel subunit alpha1 H
SNORA16A	0.923544	0.004705	0.031053	2.826564	Up	small nucleolar RNA, H/ACA box 16A
SCYL3	0.922277	0.006814	0.04082	2.705785	Up	SCY1 like pseudokinase 3
HLA-J	0.918614	1.94E-12	2.60E-10	7.038739	Up	major histocompatibility complex, class I, J (pseudogene)
CXCL2	0.917487	0.007511	0.043967	2.673279	Up	C-X-C motif chemokine ligand 2
PHF2	0.917134	0.000249	0.003226	3.663365	Up	PHD finger protein 2
TRIB2	0.911615	0.003408	0.024577	2.928347	Up	tribbles pseudokinase 2
PSMG1	0.909231	0.00298	0.022303	2.969825	Up	proteasome assembly chaperone 1
PDK4	0.90829	4.21E-06	0.000109	4.60061	Up	pyruvate dehydrogenase kinase 4
SNORD58C	0.907764	0.001022	0.009924	3.284462	Up	small nucleolar RNA, C/D box 58C
PDE4D	0.906149	0.001133	0.010707	3.255316	Up	phosphodiesterase 4D
RPS10P7	0.90502	0.001134	0.010716	3.254896	Up	ribosomal protein S10 pseudogene 7
CENPB	0.904336	0.00031	0.003844	3.606946	Up	centromere protein B
HLA-E	0.904162	6.68E-12	8.06E-10	6.864398	Up	major histocompatibility complex, class I, E
NUCB1	0.894836	8.94E-09	5.31E-07	5.749746	Up	nucleobindin 1
CHCHD10	0.894544	0.001878	0.015787	3.108808	Up	coiled-coil-helix-coiled-coil-helix domain containing 10
PLA2G4C	0.894513	0.005097	0.03286	2.800841	Up	phospholipase A2 group IVC
HLA-H	0.894171	3.72E-16	8.01E-14	8.147234	Up	major histocompatibility complex, class I, H (pseudogene)
ALDH2	0.889919	0.000355	0.004306	3.571102	Up	aldehyde dehydrogenase 2 family member
TLCD1	0.889556	0.000423	0.004945	3.525304	Up	TLC domain containing 1
QSOX1	0.889003	0.000201	0.002694	3.717941	Up	quiescin sulfhydryl oxidase 1
GNPTG	0.887892	1.68E-06	5.13E-05	4.788321	Up	N-acetylglucosamine-1-phosphate transferase subunit gamma
GAMT	0.885655	0.000914	0.009113	3.315622	Up	guanidinoacetate N-methyltransferase
MUC20	0.885387	0.003114	0.023048	2.956302	Up	mucin 20, cell surface associated
GAA	0.883575	0.000625	0.006716	3.420709	Up	glucosidase alpha, acid
EPHX1	0.882556	0.001246	0.011542	3.228161	Up	epoxide hydrolase 1
IRX2	0.87814	0.002012	0.016648	3.088401	Up	iroquois homeobox 2
KDM1B	0.877681	0.005787	0.036232	2.759592	Up	lysine demethylase 1B
AGT	0.872907	0.000369	0.00442	3.561241	Up	angiotensinogen
APOL1	0.871137	0.006065	0.037495	2.744251	Up	apolipoprotein L1
ERBB3	0.866594	0.004566	0.030436	2.836126	Up	erb-b2 receptor tyrosine kinase 3
GC	0.865249	2.64E-05	0.000509	4.202422	Up	GC vitamin D binding protein
RMRP	0.86397	0.007313	0.043044	2.682239	Up	RNA component of mitochondrial RNA processing endoribonuclease

PCSK1N	0.863171	6.05E-08	2.80E-06	5.417249	Up	proprotein convertase subtilisin/kexin type 1 inhibitor
SLC38A4	0.862664	3.30E-05	0.000608	4.151567	Up	solute carrier family 38 member 4
MLXIPL	0.858192	6.46E-05	0.001051	3.995352	Up	MLX interacting protein like
RELA	0.857395	0.001565	0.013703	3.162393	Up	RELA proto-oncogene, NF-kB subunit
ABHD14A	0.850443	0.002904	0.02186	2.97768	Up	abhydrolase domain containing 14A
C8orf82	0.850138	0.008439	0.047738	2.634	Up	chromosome 8 open reading frame 82
UNKL	0.847906	7.89E-06	0.000186	4.468256	Up	unk like zinc finger
PTPRN2	0.840172	6.24E-06	0.000152	4.51796	Up	protein tyrosine phosphatase receptor type N2
RTN1	0.837885	0.001814	0.015323	3.119108	Up	reticulon 1
FAM193B	0.835166	0.002056	0.016897	3.082015	Up	family with sequence similarity 193 member B
SLC44A4	0.830175	0.00423	0.028795	2.860443	Up	solute carrier family 44 member 4
TMEM183B	0.829275	0.000465	0.005319	3.500193	Up	transmembrane protein 183B
C4orf48	0.827987	0.000237	0.003105	3.676047	Up	chromosome 4 open reading frame 48
TBL2	0.824308	0.006363	0.038834	2.72849	Up	transducin beta like 2
CEBPD	0.822274	0.001777	0.015066	3.125176	Up	CCAAT enhancer binding protein delta
RCAN2	0.817966	0.002449	0.019362	3.029615	Up	regulator of calcineurin 2
LYZ	0.814951	0.004806	0.031556	2.819766	Up	lysozyme
IFITM2	0.813561	0.000853	0.008613	3.335119	Up	interferon induced transmembrane protein 2
FAM8A1	0.810943	0.004296	0.029143	2.855578	Up	family with sequence similarity 8 member A1
REPIN1	0.808075	0.000433	0.005031	3.519312	Up	replication initiator 1
DCAF11	0.805362	0.00197	0.016392	3.094725	Up	DDB1 and CUL4 associated factor 11
HLA-C	0.800301	3.33E-12	4.26E-10	6.962988	Up	major histocompatibility complex, class I, C
BTG1	0.800153	8.89E-09	5.30E-07	5.750679	Up	BTG anti-proliferation factor 1
RAB5C	0.797754	1.87E-05	0.000381	4.279496	Up	RAB5C, member RAS oncogene family
ARRDC4	0.79144	0.00267	0.02064	3.003382	Up	arrestin domain containing 4
HLA-A	0.789204	3.01E-15	5.65E-13	7.890626	Up	major histocompatibility complex, class I, A
PJA1	0.78577	0.007641	0.0445	2.667514	Up	praja ring finger ubiquitin ligase 1
TRIOBP	0.785496	0.004833	0.031656	2.817931	Up	TRIO and F-actin binding protein
CLU	0.784071	1.52E-11	1.70E-09	6.745903	Up	clusterin
SDHA	0.783467	0.000506	0.005656	3.477682	Up	succinate dehydrogenase complex flavoprotein subunit A
KCNK3	0.783131	0.000368	0.004415	3.561765	Up	potassium two pore domain channel subfamily K member 3
RORA	0.782585	0.002328	0.018607	3.044836	Up	RAR related orphan receptor A
GCG	0.78151	1.87E-05	0.000381	4.279675	Up	glucagon
SLC4A4	0.781078	0.003066	0.022802	2.961006	Up	solute carrier family 4 member 4
SPINT2	0.780022	9.63E-11	8.88E-09	6.472653	Up	serine peptidase inhibitor, Kunitz type 2
CFC1	0.776461	0.000113	0.001657	3.861527	Up	cripto, FRL-1, cryptic family 1
CFC1B	0.776461	0.000113	0.001657	3.861527	Up	cripto, FRL-1, cryptic family 1B
GPX3	0.773677	9.26E-07	3.06E-05	4.906725	Up	glutathione peroxidase 3
MAF	0.769808	0.001577	0.013743	3.16013	Up	MAF bZIP transcription factor
PFKL	0.768515	0.002023	0.016727	3.086839	Up	phosphofructokinase, liver type
BCS1L	0.76814	0.00669	0.040207	2.71188	Up	BCS1 homolog, ubiquinol-cytochrome c reductase complex chaperone
POLR2A	0.760606	3.80E-05	0.000676	4.119563	Up	RNA polymerase II subunit A
RNF149	0.757628	3.03E-05	0.000569	4.171111	Up	ring finger protein 149

HPS3	0.757014	0.003509	0.025028	2.919233	Up	HPS3 biogenesis of lysosomal organelles complex 2 subunit 1
ANP32A	0.756629	8.89E-05	0.001361	3.919	Up	acidic nuclear phosphoprotein 32 family member A
COA5	0.755377	0.000444	0.005122	3.512514	Up	cytochrome c oxidase assembly factor 5
PUS7L	0.752571	0.004713	0.031065	2.826015	Up	pseudouridine synthase 7 like
DACH1	0.751247	0.001646	0.014201	3.147665	Up	dachshund family transcription factor 1
RNPEP	0.75053	0.000405	0.004758	3.536608	Up	arginyl aminopeptidase
SERPINE2	0.74936	0.001499	0.013289	3.174888	Up	serpin family E member 2
LSM6	0.747747	5.05E-05	0.00086	4.053353	Up	LSM6 homolog, U6 small nuclear RNA and mRNA degradation associated
ABLIM1	0.74695	3.75E-06	9.89E-05	4.624807	Up	actin binding LIM protein 1
PPAN-P2RY11	0.745678	5.43E-05	0.000913	4.036365	Up	PPAN-P2RY11 readthrough
GET4	0.743207	0.002683	0.020717	3.001928	Up	guided entry of tail-anchored proteins factor 4
SPAG16	0.742949	0.000338	0.004142	3.584044	Up	sperm associated antigen 16
RAP1GAP	0.74019	0.001536	0.013537	3.167786	Up	RAP1 GTPase activating protein
MTMR12	0.739827	0.003094	0.022947	2.958222	Up	myotubularin related protein 12
SNN	0.739567	0.001212	0.011301	3.23615	Up	stannin
ITPK1	0.737421	0.002697	0.020771	3.000349	Up	inositol-tetrakisphosphate 1-kinase
PLTP	0.735518	1.70E-07	6.94E-06	5.229404	Up	phospholipid transfer protein
SESN1	0.733841	0.004166	0.028469	2.865326	Up	sestrin 1
CCDC86	0.732086	0.005585	0.035271	2.77121	Up	coiled-coil domain containing 86
CHGB	0.731999	5.33E-07	1.87E-05	5.014107	Up	chromogranin B
RGS4	0.731903	9.90E-05	0.001492	3.892916	Up	regulator of G protein signaling 4
CLDN7	0.729918	8.21E-05	0.001277	3.938047	Up	claudin 7
PPM1B	0.724653	0.008246	0.047041	2.641841	Up	protein phosphatase, Mg2+/Mn2+ dependent 1B
C9orf16	0.722277	0.00032	0.00394	3.598756	Up	chromosome 9 open reading frame 16
POLD2	0.72133	0.000506	0.005656	3.477682	Up	DNA polymerase delta 2, accessory subunit
CYB5R3	0.720759	2.38E-06	6.67E-05	4.718096	Up	cytochrome b5 reductase 3
TMEM176B	0.720352	1.06E-05	0.000237	4.40538	Up	transmembrane protein 176B
CMTM8	0.719692	0.008327	0.047336	2.638533	Up	CKLF like MARVEL transmembrane domain containing 8
PCSK2	0.717848	1.24E-05	0.000272	4.370337	Up	proprotein convertase subtilisin/kexin type 2
P4HA1	0.717174	0.000198	0.002659	3.721805	Up	prolyl 4-hydroxylase subunit alpha 1
RPRD1A	0.71633	0.001345	0.012208	3.206219	Up	regulation of nuclear pre-mRNA domain containing 1A
CES2	0.716072	0.001076	0.010276	3.269859	Up	carboxylesterase 2
MAN1A1	0.714242	6.27E-06	0.000152	4.516969	Up	mannosidase alpha class 1A member 1
CACNA1A	0.712675	0.001542	0.013561	3.166569	Up	calcium voltage-gated channel subunit alpha1 A
KLHL12	0.711808	0.007545	0.044081	2.671774	Up	kelch like family member 12
ID2	0.710358	3.60E-05	0.000651	4.131867	Up	inhibitor of DNA binding 2
ARHGAP12	0.709594	0.00071	0.007421	3.385629	Up	Rho GTPase activating protein 12
MOCS2	0.709439	3.97E-05	0.000701	4.109489	Up	molybdenum cofactor synthesis 2
TUSC2	0.708041	0.006864	0.041019	2.703368	Up	tumor suppressor 2, mitochondrial calcium regulator
TCEAL2	0.707716	0.002121	0.017261	3.072677	Up	transcription elongation factor A like 2
U2AF2	0.70594	0.007189	0.042501	2.687943	Up	U2 small nuclear RNA auxiliary factor 2
MGRN1	0.703772	0.00124	0.011491	3.22959	Up	mahogunin ring finger 1
PPARA	0.703065	0.005332	0.033986	2.786232	Up	peroxisome proliferator activated receptor alpha

CAPN7	0.701948	0.003625	0.025627	2.909118	Up	calpain 7
ARL6IP4	0.700483	8.56E-05	0.001313	3.928163	Up	ADP ribosylation factor like GTPase 6 interacting protein 4
ANXA4	0.700394	0.00019	0.002576	3.732303	Up	annexin A4
SUCLG2	0.70025	0.000827	0.008388	3.343483	Up	succinate-CoA ligase GDP-forming subunit beta
TFRC	0.700148	6.66E-05	0.001078	3.988234	Up	transferrin receptor
TTC39A	0.699028	0.000609	0.006568	3.427548	Up	tetratricopeptide repeat domain 39A
MRPL38	0.695461	0.007369	0.04329	2.679669	Up	mitochondrial ribosomal protein L38
TXNDC11	0.693311	0.002648	0.020521	3.005867	Up	thioredoxin domain containing 11
SLC39A1	0.687707	0.003642	0.025729	2.907625	Up	solute carrier family 39 member 1
LOC100129534	0.686772	3.72E-25	1.67E-22	10.36124	Up	small nuclear ribonucleoprotein polypeptide N pseudogene
COQ4	0.685338	0.006238	0.03831	2.735002	Up	coenzyme Q4
GALNT3	0.684973	0.002196	0.017742	3.062363	Up	polypeptide N-acetylgalactosaminyltransferase 3
LDLR	0.681819	0.000344	0.004196	3.579354	Up	low density lipoprotein receptor
BET1	0.681654	0.000455	0.005234	3.505722	Up	Bet1 golgi vesicular membrane trafficking protein
DUT	0.67494	0.000365	0.004386	3.564089	Up	deoxyuridine triphosphatase
FTH1	0.674678	9.55E-12	1.11E-09	6.813071	Up	ferritin heavy chain 1
LY75-CD302	0.672266	0.00339	0.024517	2.930009	Up	LY75-CD302 readthrough
SSBP3	0.66799	0.005563	0.035169	2.772481	Up	single stranded DNA binding protein 3
ARHGEF10L	0.664155	0.008544	0.048154	2.629762	Up	Rho guanine nucleotide exchange factor 10 like
SLMAP	0.663003	0.001703	0.014549	3.137686	Up	sarcolemma associated protein
PGRMC1	0.661335	0.000753	0.007766	3.36948	Up	progesterone receptor membrane component 1
HLA-F	0.659739	3.46E-05	0.00063	4.140949	Up	major histocompatibility complex, class I, F
SEC24B	0.658743	0.004881	0.031836	2.814813	Up	SEC24 homolog B, COPII coat complex component
PPP1CC	0.652481	0.00073	0.007589	3.378032	Up	protein phosphatase 1 catalytic subunit gamma
CCDC152	0.651268	0.004007	0.027622	2.877578	Up	coiled-coil domain containing 152
STAMBP	0.648299	0.00318	0.023371	2.949738	Up	STAM binding protein
DPP7	0.644342	0.004665	0.030928	2.829281	Up	dipeptidyl peptidase 7
CD81	0.644011	8.52E-06	0.000199	4.451719	Up	CD81 molecule
AK1	0.64326	0.002527	0.019794	3.020081	Up	adenylate kinase 1
SEMA4B	0.642691	0.005039	0.032592	2.804522	Up	semaphorin 4B
HIF1A	0.641721	5.37E-06	0.000134	4.54991	Up	hypoxia inducible factor 1 subunit alpha
GPAA1	0.640751	0.00177	0.015039	3.126294	Up	glycosylphosphatidylinositol anchor attachment 1
SLC25A36	0.637235	0.002624	0.02039	3.008665	Up	solute carrier family 25 member 36
CCDC18	0.635747	0.003935	0.027279	2.883347	Up	coiled-coil domain containing 18
CPLX2	0.634062	0.006991	0.041576	2.697274	Up	complexin 2
GGA2	0.633393	0.000806	0.008195	3.350871	Up	golgi associated, gamma adaptin ear containing, ARF binding protein 2
GIGYF1	0.63099	1.35E-05	0.000292	4.35222	Up	GRB10 interacting GYF protein 1
SULT1E1	-8.16887	1.02E-44	1.17E-41	-14.0299	Down	sulfotransferase family 1E member 1
SEMA3C	-6.99712	3.64E-53	6.76E-50	-15.3482	Down	semaphorin 3C
ISLR	-6.99695	1.69E-65	1.25E-61	-17.0924	Down	immunoglobulin superfamily containing leucine rich repeat
PCK1	-6.8013	5.06E-39	4.18E-36	-13.0673	Down	phosphoenolpyruvate carboxykinase 1
KRT17	-6.28089	3.08E-45	3.81E-42	-14.1148	Down	keratin 17
IGF2BP3	-5.85349	6.87E-36	5.10E-33	-12.5066	Down	insulin like growth factor 2 mRNA binding protein 3

TDO2	-5.56834	5.84E-33	3.61E-30	-11.9588	Down	tryptophan 2,3-dioxygenase
POSTN	-5.43333	8.15E-47	1.10E-43	-14.3686	Down	periostin
COL6A3	-5.35601	6.96E-88	1.03E-83	-19.8731	Down	collagen type VI alpha 3 chain
SOX11	-5.00018	2.19E-33	1.42E-30	-12.0398	Down	SRY-box transcription factor 11
KRT6B	-4.96583	7.73E-12	9.11E-10	-6.8434	Down	keratin 6B
IL1RL1	-4.95954	1.75E-06	5.29E-05	-4.78075	Down	interleukin 1 receptor like 1
BNC2	-4.91463	1.36E-28	6.73E-26	-11.0928	Down	basonuclin 2
SLCO2A1	-4.86935	2.68E-17	6.53E-15	-8.4597	Down	solute carrier organic anion transporter family member 2A1
TAGLN	-4.73723	1.06E-38	8.25E-36	-13.0113	Down	transgelin
S1PR1	-4.72945	9.65E-10	7.03E-08	-6.11507	Down	sphingosine-1-phosphate receptor 1
NRG3	-4.7291	6.74E-08	3.07E-06	-5.39788	Down	neuregulin 3
GJC1	-4.70503	2.40E-30	1.32E-27	-11.4482	Down	gap junction protein gamma 1
NTM	-4.63089	3.87E-18	1.06E-15	-8.68256	Down	neurotrimin
ST6GAL2	-4.60433	2.92E-15	5.55E-13	-7.89441	Down	ST6 beta-galactoside alpha-2,6-sialyltransferase 2
CSF2	-4.59632	1.14E-11	1.31E-09	-6.78722	Down	colony stimulating factor 2
SULF1	-4.52079	1.82E-42	1.93E-39	-13.6575	Down	sulfatase 1
CD34	-4.493	1.30E-14	2.33E-12	-7.70548	Down	CD34 molecule
RASSF2	-4.42796	1.18E-13	1.85E-11	-7.41871	Down	Ras association domain family member 2
ACTA2	-4.36581	4.29E-39	3.74E-36	-13.08	Down	actin alpha 2, smooth muscle
TOP2A	-4.363	4.09E-12	5.15E-10	-6.9339	Down	DNA topoisomerase II alpha
CENPE	-4.35643	4.63E-08	2.25E-06	-5.46505	Down	centromere protein E
ESM1	-4.33455	7.61E-10	5.68E-08	-6.15282	Down	endothelial cell specific molecule 1
ADAMTS12	-4.31989	6.88E-17	1.57E-14	-8.34908	Down	ADAM metallopeptidase with thrombospondin type 1 motif 12
TGFBI	-4.31696	6.45E-49	9.58E-46	-14.7	Down	transforming growth factor beta induced
OLFML1	-4.29731	2.09E-10	1.79E-08	-6.35473	Down	olfactomedin like 1
GJA4	-4.28558	1.78E-05	0.000365	-4.29121	Down	gap junction protein alpha 4
CLIC5	-4.25197	1.80E-08	9.94E-07	-5.63015	Down	chloride intracellular channel 5
OLFML3	-4.24213	2.40E-13	3.59E-11	-7.32459	Down	olfactomedin like 3
COL3A1	-4.19955	1.49E-54	3.70E-51	-15.554	Down	collagen type III alpha 1 chain
EGF	-4.18772	1.09E-12	1.50E-10	-7.11819	Down	epidermal growth factor
MUC4	-4.18467	5.87E-06	0.000144	-4.53109	Down	mucin 4, cell surface associated
COL1A2	-4.17512	1.54E-55	4.59E-52	-15.6987	Down	collagen type I alpha 2 chain
FN1	-4.17427	8.36E-63	4.14E-59	-16.7268	Down	fibronectin 1
LUM	-4.1577	1.94E-40	1.80E-37	-13.313	Down	lumican
SPARC	-4.14871	5.75E-57	2.13E-53	-15.9061	Down	secreted protein acidic and cysteine rich
FRZB	-4.1365	8.96E-10	6.58E-08	-6.12698	Down	frizzled related protein
COL5A1	-4.12837	1.48E-28	6.93E-26	-11.0849	Down	collagen type V alpha 1 chain
THY1	-4.09014	8.03E-25	3.51E-22	-10.2874	Down	Thy-1 cell surface antigen
EMCN	-4.0853	8.78E-11	8.34E-09	-6.48654	Down	endomucin
PECAM1	-4.06447	4.57E-13	6.79E-11	-7.23754	Down	platelet and endothelial cell adhesion molecule 1
GAP43	-4.00349	6.11E-19	1.85E-16	-8.88993	Down	growth associated protein 43
ASB9	-3.99904	6.65E-29	3.40E-26	-11.1566	Down	ankyrin repeat and SOCS box containing 9
AFAP1L1	-3.99574	1.57E-07	6.51E-06	-5.24426	Down	actin filament associated protein 1 like 1

XAF1	-3.96621	7.76E-15	1.44E-12	-7.77142	Down	XIAP associated factor 1
SRPX	-3.9576	8.61E-10	6.36E-08	-6.13322	Down	sushi repeat containing protein X-linked
HEPH	-3.94057	1.14E-08	6.66E-07	-5.70859	Down	hephaestin
BCAS1	-3.91979	2.94E-06	7.98E-05	-4.67529	Down	brain enriched myelin associated protein 1
NES	-3.90754	1.59E-15	3.14E-13	-7.96988	Down	nestin
FABP4	-3.90568	4.07E-11	4.17E-09	-6.60142	Down	fatty acid binding protein 4
CST6	-3.89561	1.18E-07	5.03E-06	-5.29674	Down	cystatin E/M
CD248	-3.88898	5.14E-12	6.34E-10	-6.90153	Down	CD248 molecule
PTGS2	-3.86934	2.65E-19	8.51E-17	-8.9824	Down	prostaglandin-endoperoxide synthase 2
ENPEP	-3.85123	1.95E-06	5.75E-05	-4.7584	Down	glutamyl aminopeptidase
LTB4R	-3.84992	6.75E-07	2.30E-05	-4.96848	Down	leukotriene B4 receptor
ITGA11	-3.8315	2.63E-10	2.22E-08	-6.31901	Down	integrin subunit alpha 11
IGDCC4	-3.82989	6.78E-17	1.57E-14	-8.35083	Down	immunoglobulin superfamily DCC subclass member 4
SPOCD1	-3.82989	4.20E-08	2.08E-06	-5.48232	Down	SPOC domain containing 1
VCAN	-3.82926	1.49E-28	6.93E-26	-11.0844	Down	versican
MFAP2	-3.82601	2.21E-20	7.63E-18	-9.25168	Down	microfibril associated protein 2
PI15	-3.81639	1.29E-11	1.45E-09	-6.76976	Down	peptidase inhibitor 15
COL1A1	-3.81542	2.97E-50	4.90E-47	-14.907	Down	collagen type I alpha 1 chain
HHATL	-3.81056	2.62E-08	1.38E-06	-5.56493	Down	hedgehog acyltransferase like
LRRC17	-3.78527	1.35E-09	9.35E-08	-6.06157	Down	leucine rich repeat containing 17
FHOD3	-3.77153	5.30E-12	6.45E-10	-6.89726	Down	formin homology 2 domain containing 3
DACT1	-3.75494	1.10E-10	9.99E-09	-6.45208	Down	dishevelled binding antagonist of beta catenin 1
PIEZO2	-3.73731	1.53E-15	3.07E-13	-7.97465	Down	piezo type mechanosensitive ion channel component 2
REP15	-3.72234	2.11E-07	8.40E-06	-5.18894	Down	RAB15 effector protein
CPA4	-3.69821	2.45E-12	3.19E-10	-7.00608	Down	carboxypeptidase A4
NID1	-3.67312	1.68E-18	4.79E-16	-8.77708	Down	nidogen 1
PRSS12	-3.65724	1.30E-15	2.64E-13	-7.9947	Down	serine protease 12
GUCY1A2	-3.64287	3.48E-05	0.000633	-4.13939	Down	guanylate cyclase 1 soluble subunit alpha 2
HAS2	-3.61739	5.44E-21	2.07E-18	-9.40026	Down	hyaluronan synthase 2
TMEM233	-3.61228	0.001142	0.010766	-3.25303	Down	transmembrane protein 233
ADA	-3.60883	2.18E-13	3.31E-11	-7.33707	Down	adenosine deaminase
LDHAL6A	-3.60004	5.92E-06	0.000145	-4.5294	Down	lactate dehydrogenase A like 6A
PALMD	-3.59649	7.10E-08	3.23E-06	-5.38855	Down	palmdelphin
FIBIN	-3.57473	5.38E-08	2.57E-06	-5.43815	Down	fin bud initiation factor homolog
ARG1	-3.57404	0.005807	0.036311	-2.75847	Down	arginase 1
CDH13	-3.56691	3.89E-05	0.000691	-4.11376	Down	cadherin 13
CDH11	-3.48989	8.32E-21	3.01E-18	-9.35553	Down	cadherin 11
BMP4	-3.48514	2.37E-08	1.26E-06	-5.58236	Down	bone morphogenetic protein 4
HCLS1	-3.48103	6.80E-07	2.31E-05	-4.96694	Down	hematopoietic cell-specific Lyn substrate 1
HSF2BP	-3.4663	0.002364	0.01882	-3.0402	Down	heat shock transcription factor 2 binding protein
KIF2C	-3.46461	0.00019	0.002576	-3.73201	Down	kinesin family member 2C
CMAHP	-3.4563	0.000365	0.004386	-3.56411	Down	cytidine monophospho-N-acetylneuraminic acid hydroxylase, pseudogene
CCNJL	-3.44621	3.38E-05	0.00062	-4.14601	Down	cyclin J like

COL12A1	-3.43746	6.71E-13	9.40E-11	-7.18524	Down	collagen type XII alpha 1 chain
PLXDC1	-3.42606	6.77E-09	4.17E-07	-5.79652	Down	plexin domain containing 1
FLI1	-3.42332	0.000294	0.003672	-3.62093	Down	Fli-1 proto-oncogene, ETS transcription factor
SLC2A2	-3.42142	1.23E-08	7.10E-07	-5.6957	Down	solute carrier family 2 member 2
MEG8	-3.41669	1.00E-05	0.000226	-4.41685	Down	maternally expressed 8, small nucleolar RNA host gene
FLNC	-3.41112	0.000175	0.002423	-3.75208	Down	filamin C
ALPK2	-3.40152	0.00075	0.007745	-3.37063	Down	alpha kinase 2
SST	-3.37446	1.81E-53	3.83E-50	-15.3936	Down	somatostatin
BTN2A2	-3.36353	3.62E-11	3.73E-09	-6.61885	Down	butyrophilin subfamily 2 member A2
CYBRD1	-3.35493	6.77E-12	8.11E-10	-6.86235	Down	cytochrome b reductase 1
BUB1	-3.35131	0.00012	0.001749	-3.84637	Down	BUB1 mitotic checkpoint serine/threonine kinase
STRA6	-3.35023	1.39E-07	5.85E-06	-5.2665	Down	signaling receptor and transporter of retinol STRA6
PTHLH	-3.34655	1.42E-08	8.09E-07	-5.67072	Down	parathyroid hormone like hormone
TULP2	-3.33857	4.38E-10	3.55E-08	-6.24001	Down	TUB like protein 2
LEF1	-3.33571	6.25E-07	2.16E-05	-4.98345	Down	lymphoid enhancer binding factor 1
GLI2	-3.32111	9.92E-07	3.26E-05	-4.89315	Down	GLI family zinc finger 2
POU2F2	-3.31154	2.21E-06	6.35E-05	-4.73306	Down	POU class 2 homeobox 2
ZFHX4	-3.30289	6.86E-11	6.70E-09	-6.52373	Down	zinc finger homeobox 4
VGLL3	-3.29299	5.04E-16	1.07E-13	-8.11063	Down	vestigial like family member 3
ADAMTS6	-3.27426	7.88E-16	1.65E-13	-8.05597	Down	ADAM metallopeptidase with thrombospondin type 1 motif 6
SRPX2	-3.27082	8.78E-20	2.90E-17	-9.10308	Down	sushi repeat containing protein X-linked 2
TNFAIP6	-3.27015	1.41E-23	5.97E-21	-10.0079	Down	TNF alpha induced protein 6
UPK1B	-3.26379	2.81E-06	7.70E-05	-4.68427	Down	uroplakin 1B
DDX43	-3.26053	0.000486	0.005496	-3.4881	Down	DEAD-box helicase 43
P4HA3	-3.25419	2.56E-05	0.000497	-4.20961	Down	prolyl 4-hydroxylase subunit alpha 3
ADAM28	-3.25015	1.68E-05	0.000349	-4.30313	Down	ADAM metallopeptidase domain 28
RPA4	-3.23437	0.002467	0.019475	-3.02739	Down	replication protein A4
GIMAP7	-3.23156	0.000937	0.009301	-3.30879	Down	GTPase, IMAP family member 7
COL22A1	-3.23086	0.001317	0.012041	-3.21229	Down	collagen type XXII alpha 1 chain
BGN	-3.22635	1.70E-23	7.02E-21	-9.98901	Down	biglycan
BPIFC	-3.21015	0.006092	0.037603	-2.74277	Down	BPI fold containing family C
IL18	-3.20589	8.09E-11	7.80E-09	-6.49886	Down	interleukin 18
GPC3	-3.20357	5.22E-06	0.000131	-4.55581	Down	glypican 3
CD93	-3.19308	5.91E-08	2.76E-06	-5.42147	Down	CD93 molecule
PGF	-3.19231	1.25E-05	0.000273	-4.36831	Down	placental growth factor
PLEKHG1	-3.18607	4.24E-10	3.48E-08	-6.24488	Down	pleckstrin homology and RhoGEF domain containing G1
CMTM3	-3.18497	5.80E-20	1.96E-17	-9.14799	Down	CKLF like MARVEL transmembrane domain containing 3
CTSK	-3.16971	1.64E-17	4.35E-15	-8.51671	Down	cathepsin K
GRIP1	-3.16616	6.42E-10	4.89E-08	-6.17974	Down	glutamate receptor interacting protein 1
S1PR3	-3.16211	6.70E-10	5.07E-08	-6.17307	Down	sphingosine-1-phosphate receptor 3
CNGA3	-3.15833	4.78E-10	3.82E-08	-6.22618	Down	cyclic nucleotide gated channel subunit alpha 3
ADAMTS16	-3.15294	1.09E-05	0.000243	-4.39764	Down	ADAM metallopeptidase with thrombospondin type 1 motif 16
LAMA1	-3.15139	1.14E-05	0.000253	-4.38889	Down	laminin subunit alpha 1

A2M	-3.14799	2.96E-17	7.09E-15	-8.44816	Down	alpha-2-macroglobulin
MYCT1	-3.12838	2.80E-05	0.000535	-4.18913	Down	MYC target 1
LRRC70	-3.12174	3.67E-05	0.000657	-4.12742	Down	leucine rich repeat containing 70
ST8SIA4	-3.12163	2.25E-08	1.21E-06	-5.59122	Down	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4
COL5A2	-3.11416	1.22E-20	4.31E-18	-9.31513	Down	collagen type V alpha 2 chain
DGKI	-3.10767	1.70E-05	0.000352	-4.30088	Down	diacylglycerol kinase iota
NETO2	-3.10713	7.23E-05	0.00115	-3.96847	Down	neuropilin and tolloid like 2
SNAI2	-3.09547	2.95E-11	3.08E-09	-6.64921	Down	snail family transcriptional repressor 2
UNC5D	-3.09533	5.19E-10	4.08E-08	-6.21334	Down	unc-5 netrin receptor D
TRIM36	-3.09527	0.000179	0.002459	-3.74687	Down	tripartite motif containing 36
COL14A1	-3.09404	4.86E-05	0.000836	-4.06217	Down	collagen type XIV alpha 1 chain
EBF1	-3.06903	5.45E-13	7.94E-11	-7.21355	Down	EBF transcription factor 1
VAT1L	-3.06878	1.32E-09	9.21E-08	-6.0648	Down	vesicle amine transport 1 like
EPHB6	-3.06128	6.62E-07	2.27E-05	-4.97217	Down	EPH receptor B6
ALK	-3.05586	2.28E-06	6.49E-05	-4.72653	Down	ALK receptor tyrosine kinase
GHRL	-3.05351	1.65E-11	1.81E-09	-6.73366	Down	ghrelin and obestatin prepropeptide
HEY2	-3.04581	0.001033	0.009991	-3.28144	Down	hes related family bHLH transcription factor with YRPW motif 2
FBN1	-3.04283	2.19E-16	4.85E-14	-8.21132	Down	fibrillin 1
SLC7A5	-3.0307	3.65E-16	7.97E-14	-8.14962	Down	solute carrier family 7 member 5
RASIP1	-3.0253	1.38E-05	0.000297	-4.34762	Down	Ras interacting protein 1
CDK1	-3.01086	0.001964	0.016358	-3.09569	Down	cyclin dependent kinase 1
C1orf54	-3.00335	1.08E-09	7.70E-08	-6.09648	Down	chromosome 1 open reading frame 54
SLC9A9	-2.99945	3.67E-07	1.37E-05	-5.08539	Down	solute carrier family 9 member A9
SOX7	-2.99541	3.92E-05	0.000694	-4.1124	Down	SRY-box transcription factor 7
TET1	-2.98965	2.86E-09	1.88E-07	-5.93916	Down	tet methylcytosine dioxygenase 1
TMPRSS11E	-2.97933	0.002569	0.020043	-3.01511	Down	transmembrane serine protease 11E
MGP	-2.97256	1.24E-14	2.27E-12	-7.71206	Down	matrix Gla protein
RAB38	-2.97255	0.002875	0.021699	-2.98083	Down	RAB38, member RAS oncogene family
HOXA3	-2.9662	1.47E-05	0.00031	-4.33381	Down	homeobox A3
F2R	-2.96073	1.37E-13	2.12E-11	-7.3993	Down	coagulation factor II thrombin receptor
GGT5	-2.95488	1.87E-06	5.57E-05	-4.7675	Down	gamma-glutamyltransferase 5
ANO1	-2.94931	3.19E-07	1.21E-05	-5.11161	Down	anoctamin 1
TPX2	-2.94516	0.000244	0.003179	-3.66887	Down	TPX2 microtubule nucleation factor
KCNH7	-2.94502	2.84E-05	0.00054	-4.1863	Down	potassium voltage-gated channel subfamily H member 7
ECSCR	-2.93745	0.000713	0.007436	-3.38472	Down	endothelial cell surface expressed chemotaxis and apoptosis regulator
SALL4	-2.92459	1.19E-06	3.84E-05	-4.85668	Down	spalt like transcription factor 4
EDNRA	-2.92262	6.19E-10	4.76E-08	-6.18556	Down	endothelin receptor type A
LTBP2	-2.91196	4.94E-13	7.26E-11	-7.22705	Down	latent transforming growth factor beta binding protein 2
DLL4	-2.91058	2.82E-14	4.77E-12	-7.6061	Down	delta like canonical Notch ligand 4
MMP3	-2.90798	2.23E-06	6.38E-05	-4.73179	Down	matrix metallopeptidase 3
TBC1D2	-2.8974	0.000753	0.007766	-3.36966	Down	TBC1 domain family member 2
AGPAT4-IT1	-2.89031	2.87E-05	0.000544	-4.18382	Down	AGPAT4 intronic transcript 1
KIT	-2.89029	1.92E-06	5.69E-05	-4.76181	Down	KIT proto-oncogene, receptor tyrosine kinase

ECM2	-2.8828	6.75E-05	0.00109	-3.98476	Down	extracellular matrix protein 2
KANK4	-2.88067	2.26E-08	1.21E-06	-5.59113	Down	KN motif and ankyrin repeat domains 4
GLIPR1L2	-2.87857	6.40E-05	0.001042	-3.99754	Down	GLIPR1 like 2
PLA2R1	-2.87806	0.001	0.009746	-3.29066	Down	phospholipase A2 receptor 1
FAT3	-2.87436	5.46E-05	0.000915	-4.03496	Down	FAT atypical cadherin 3
CLEC4A	-2.87294	5.63E-08	2.65E-06	-5.43021	Down	C-type lectin domain family 4 member A
ARHGAP25	-2.86511	0.001001	0.009757	-3.29016	Down	Rho GTPase activating protein 25
SLC17A6	-2.86505	1.70E-09	1.16E-07	-6.02454	Down	solute carrier family 17 member 6
PCDH12	-2.85982	0.001587	0.013797	-3.15831	Down	protocadherin 12
NELL2	-2.8545	8.54E-06	0.000199	-4.45114	Down	neural EGFL like 2
ITM2A	-2.84768	2.86E-05	0.000544	-4.18436	Down	integral membrane protein 2A
NID2	-2.84571	1.32E-18	3.84E-16	-8.80424	Down	nidogen 2
SPATA9	-2.84139	0.00542	0.034441	-2.78094	Down	spermatogenesis associated 9
SGCD	-2.84061	8.87E-11	8.34E-09	-6.48501	Down	sarcoglycan delta
LFNG	-2.83599	1.25E-07	5.31E-06	-5.28574	Down	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase
HLA-DQB1	-2.83038	2.70E-06	7.45E-05	-4.69216	Down	major histocompatibility complex, class II, DQ beta 1
MMRN2	-2.8234	0.000835	0.008454	-3.34107	Down	multimerin 2
ZNF792	-2.81878	0.002122	0.017261	-3.07254	Down	zinc finger protein 792
ZBTB47	-2.81672	8.84E-11	8.34E-09	-6.48554	Down	zinc finger and BTB domain containing 47
SHF	-2.81445	0.001202	0.011223	-3.2385	Down	Src homology 2 domain containing F
STOX2	-2.81284	2.67E-07	1.04E-05	-5.14502	Down	storkhead box 2
HRH1	-2.80952	0.001428	0.012824	-3.18885	Down	histamine receptor H1
KIF6	-2.80909	0.00234	0.018683	-3.04329	Down	kinesin family member 6
TMSB15A	-2.80489	0.003508	0.025028	-2.91935	Down	thymosin beta 15A
TIMP3	-2.8038	4.86E-29	2.58E-26	-11.1845	Down	TIMP metallopeptidase inhibitor 3
ECM1	-2.79117	5.29E-09	3.33E-07	-5.83785	Down	extracellular matrix protein 1
EFNB2	-2.78262	3.18E-10	2.64E-08	-6.28971	Down	ephrin B2
GSTM1	-2.78072	1.01E-09	7.27E-08	-6.10804	Down	glutathione S-transferase mu 1
PCDH18	-2.7784	1.12E-07	4.83E-06	-5.30644	Down	protocadherin 18
NEXN	-2.77765	1.09E-12	1.50E-10	-7.11905	Down	nexilin F-actin binding protein
L1TD1	-2.77685	0.005073	0.032755	-2.80235	Down	LINE1 type transposase domain containing 1
SV2B	-2.77498	1.79E-07	7.22E-06	-5.21948	Down	synaptic vesicle glycoprotein 2B
SOX18	-2.76804	0.006074	0.037528	-2.74375	Down	SRY-box transcription factor 18
MXRA8	-2.76766	5.24E-07	1.85E-05	-5.01738	Down	matrix remodeling associated 8
LRRC8E	-2.7564	0.000417	0.004875	-3.52935	Down	leucine rich repeat containing 8 VRAC subunit E
MME	-2.7491	0.000693	0.007326	-3.39227	Down	membrane metalloendopeptidase
ADORA2B	-2.74876	5.74E-05	0.000957	-4.02315	Down	adenosine A2b receptor
SYNGR3	-2.7427	0.000291	0.003655	-3.62343	Down	synaptogyrin 3
LAMA4	-2.74251	2.56E-14	4.37E-12	-7.61889	Down	laminin subunit alpha 4
TAF4B	-2.73821	0.000393	0.004653	-3.545	Down	TATA-box binding protein associated factor 4b
THBS1	-2.73673	7.95E-21	2.95E-18	-9.36034	Down	thrombospondin 1
SERPIND1	-2.73469	0.004266	0.028995	-2.85777	Down	serpin family D member 1
IL16	-2.72384	3.78E-06	9.95E-05	-4.62289	Down	interleukin 16

CDKN3	-2.72285	0.004623	0.030704	-2.83218	Down	cyclin dependent kinase inhibitor 3
SYNPO2	-2.7177	0.000514	0.005736	-3.47327	Down	synaptopodin 2
ECEL1	-2.71388	6.05E-06	0.000147	-4.52456	Down	endothelin converting enzyme like 1
PDGFB	-2.69036	5.23E-07	1.85E-05	-5.01779	Down	platelet derived growth factor subunit B
UBE2C	-2.68901	0.002195	0.017742	-3.06256	Down	ubiquitin conjugating enzyme E2 C
HCST	-2.68161	0.000187	0.002549	-3.7358	Down	hematopoietic cell signal transducer
TMEM150C	-2.67938	4.09E-08	2.04E-06	-5.48704	Down	transmembrane protein 150C
OLFML2B	-2.66936	3.75E-05	0.000671	-4.12246	Down	olfactomedin like 2B
COLQ	-2.66494	2.65E-05	0.000511	-4.20122	Down	collagen like tail subunit of asymmetric acetylcholinesterase
STIL	-2.66382	0.000424	0.004948	-3.52458	Down	STIL centriolar assembly protein
MCM6	-2.66171	6.57E-08	3.00E-06	-5.40261	Down	minichromosome maintenance complex component 6
BEND6	-2.65803	0.00165	0.014228	-3.14695	Down	BEN domain containing 6
PXDN	-2.65789	1.77E-17	4.61E-15	-8.50802	Down	peroxidasin
RIPK3	-2.65386	9.93E-06	0.000224	-4.41867	Down	receptor interacting serine/threonine kinase 3
ASPM	-2.65337	0.005797	0.036279	-2.75903	Down	assembly factor for spindle microtubules
GHRLOS	-2.64408	2.47E-07	9.68E-06	-5.15983	Down	ghrelin opposite strand/antisense RNA
MSRB3	-2.6411	3.65E-08	1.85E-06	-5.50705	Down	methionine sulfoxide reductase B3
HMGA2	-2.64083	0.000876	0.008816	-3.32752	Down	high mobility group AT-hook 2
TRIM45	-2.63708	1.20E-08	6.99E-07	-5.69971	Down	tripartite motif containing 45
ATP6V1E2	-2.63692	0.003308	0.024094	-2.93754	Down	ATPase H+ transporting V1 subunit E2
SIX2	-2.63471	7.28E-05	0.001155	-3.96686	Down	SIX homeobox 2
ABI3BP	-2.63028	6.04E-10	4.67E-08	-6.18938	Down	ABI family member 3 binding protein
GDPD5	-2.6276	1.02E-05	0.000231	-4.41198	Down	glycerophosphodiester phosphodiesterase domain containing 5
PGM2	-2.62683	1.85E-12	2.50E-10	-7.04523	Down	phosphoglucomutase 2
INHBE	-2.62503	0.004887	0.031838	-2.81439	Down	inhibin subunit beta E
SLC1A3	-2.62355	0.005447	0.03458	-2.77934	Down	solute carrier family 1 member 3
GLRA1	-2.62355	4.43E-06	0.000113	-4.59034	Down	glycine receptor alpha 1
WNT5B	-2.62164	0.001625	0.014049	-3.15143	Down	Wnt family member 5B
PTN	-2.61945	0.002944	0.022103	-2.97351	Down	pleiotrophin
ZNF221	-2.61559	0.000133	0.001914	-3.82135	Down	zinc finger protein 221
SNX30	-2.60435	3.60E-14	5.88E-12	-7.57466	Down	sorting nexin family member 30
LRRC2	-2.60302	0.001772	0.015046	-3.12599	Down	leucine rich repeat containing 2
SLC16A10	-2.59549	0.001137	0.010732	-3.25427	Down	solute carrier family 16 member 10
E2F7	-2.59406	0.003671	0.025888	-2.90509	Down	E2F transcription factor 7
COL15A1	-2.58589	1.77E-13	2.71E-11	-7.36502	Down	collagen type XV alpha 1 chain
CECR2	-2.57882	0.001106	0.010498	-3.26199	Down	CECR2 histone acetyl-lysine reader
GAL	-2.5777	1.81E-05	0.00037	-4.28761	Down	galanin and GMAP prepropeptide
RSPH9	-2.57587	7.46E-06	0.000176	-4.48025	Down	radial spoke head component 9
GREM2	-2.57338	0.001316	0.012041	-3.21236	Down	gremlin 2, DAN family BMP antagonist
ULBP1	-2.56108	8.10E-06	0.00019	-4.46259	Down	UL16 binding protein 1
ADAMTS2	-2.55522	2.83E-10	2.37E-08	-6.30783	Down	ADAM metallopeptidase with thrombospondin type 1 motif 2
TNFRSF11B	-2.55422	1.05E-15	2.16E-13	-8.02144	Down	TNF receptor superfamily member 11b
PDGFRA	-2.55277	1.38E-06	4.33E-05	-4.82788	Down	platelet derived growth factor receptor alpha

ANKRD1	-2.55247	1.64E-06	5.02E-05	-4.79397	Down	ankyrin repeat domain 1
ZSCAN5A	-2.5507	0.000186	0.002532	-3.73795	Down	zinc finger and SCAN domain containing 5A
ANLN	-2.54686	0.00894	0.049674	-2.61436	Down	anillin actin binding protein
CALCRL	-2.5459	6.67E-05	0.001078	-3.98793	Down	calcitonin receptor like receptor
PTCHD1	-2.53207	0.008784	0.049131	-2.62035	Down	patched domain containing 1
COL5A3	-2.53127	4.02E-05	0.000709	-4.10631	Down	collagen type V alpha 3 chain
TUBB2B	-2.52603	1.88E-15	3.66E-13	-7.94933	Down	tubulin beta 2B class IIb
CDH5	-2.5235	0.000309	0.003837	-3.60762	Down	cadherin 5
LOX	-2.5188	2.50E-07	9.77E-06	-5.15766	Down	lysyl oxidase
COL4A1	-2.51738	4.87E-17	1.15E-14	-8.38969	Down	collagen type IV alpha 1 chain
ARHGEF10	-2.51681	6.61E-06	0.000159	-4.50591	Down	Rho guanine nucleotide exchange factor 10
MFGE8	-2.51447	1.59E-07	6.58E-06	-5.24136	Down	milk fat globule EGF and factor V/VIII domain containing
AEBP1	-2.50754	4.36E-10	3.55E-08	-6.2407	Down	AE binding protein 1
TRIM9	-2.50587	6.64E-11	6.53E-09	-6.52855	Down	tripartite motif containing 9
ZNF300	-2.50558	4.35E-06	0.000112	-4.59401	Down	zinc finger protein 300
ERG	-2.50536	0.000161	0.002256	-3.77336	Down	ETS transcription factor ERG
SLC22A3	-2.5052	0.000534	0.005923	-3.46328	Down	solute carrier family 22 member 3
FRMD5	-2.50177	0.001268	0.011698	-3.22323	Down	FERM domain containing 5
GLIPR2	-2.50019	2.91E-14	4.85E-12	-7.60241	Down	GLI pathogenesis related 2
PADI2	-2.49886	0.002365	0.01882	-3.04012	Down	peptidyl arginine deiminase 2
TK1	-2.49497	8.31E-05	0.001288	-3.93535	Down	thymidine kinase 1
DCAF4L1	-2.4942	0.000198	0.002659	-3.72214	Down	DDB1 and CUL4 associated factor 4 like 1
CNTNAP2	-2.49282	0.005935	0.036859	-2.75137	Down	contactin associated protein 2
TNFAIP8L1	-2.49185	2.31E-06	6.52E-05	-4.72453	Down	TNF alpha induced protein 8 like 1
ZC4H2	-2.49002	7.59E-08	3.42E-06	-5.37653	Down	zinc finger C4H2-type containing
ANKRD7	-2.48969	0.000358	0.004334	-3.56895	Down	ankyrin repeat domain 7
ZKSCAN3	-2.48914	0.000748	0.007729	-3.37138	Down	zinc finger with KRAB and SCAN domains 3
MMP9	-2.48823	2.21E-05	0.000438	-4.24242	Down	matrix metallopeptidase 9
PGAM2	-2.48601	0.002059	0.016911	-3.08159	Down	phosphoglycerate mutase 2
FFAR2	-2.4797	0.000571	0.00625	-3.44516	Down	free fatty acid receptor 2
CDR1	-2.47829	2.58E-06	7.17E-05	-4.70155	Down	cerebellar degeneration related protein 1
KLHL25	-2.47258	0.000631	0.006766	-3.41812	Down	kelch like family member 25
ZNF16	-2.47235	4.04E-06	0.000105	-4.60933	Down	zinc finger protein 16
TCF7	-2.4718	2.01E-08	1.08E-06	-5.61122	Down	transcription factor 7
MMS22L	-2.47167	1.14E-08	6.66E-07	-5.70884	Down	MMS22 like, DNA repair protein
PHLDA1	-2.46355	4.09E-19	1.27E-16	-8.93438	Down	pleckstrin homology like domain family A member 1
SULT4A1	-2.46335	1.73E-07	7.04E-06	-5.2257	Down	sulfotransferase family 4A member 1
GTDC1	-2.46248	1.90E-06	5.65E-05	-4.76341	Down	glycosyltransferase like domain containing 1
PCDH7	-2.46229	7.44E-12	8.84E-10	-6.84888	Down	protocadherin 7
COL6A2	-2.45951	1.34E-06	4.22E-05	-4.83439	Down	collagen type VI alpha 2 chain
HSD3BP4	-2.45746	0.000403	0.004737	-3.53824	Down	hydroxy-delta-5-steroid dehydrogenase, 3 beta, pseudogene 4
KDR	-2.45267	9.46E-05	0.001435	-3.90403	Down	kinase insert domain receptor
MYL9	-2.45098	5.12E-10	4.04E-08	-6.21545	Down	myosin light chain 9

NRBP2	-2.44931	5.08E-07	1.81E-05	-5.02323	Down	nuclear receptor binding protein 2
SERPINE1	-2.44289	2.10E-17	5.38E-15	-8.48813	Down	serpin family E member 1
CDH6	-2.4343	1.27E-08	7.31E-07	-5.6895	Down	cadherin 6
DCHS1	-2.43327	5.12E-07	1.82E-05	-5.02175	Down	dachsous cadherin-related 1
KIF26B	-2.43288	4.55E-05	0.000788	-4.0775	Down	kinesin family member 26B
ZRANB3	-2.42846	3.91E-07	1.44E-05	-5.07349	Down	zinc finger RANBP2-type containing 3
GPR161	-2.42658	3.29E-05	0.000606	-4.15258	Down	G protein-coupled receptor 161
NTNG2	-2.42597	2.30E-07	9.03E-06	-5.17351	Down	netrin G2
ACOX2	-2.42189	0.003694	0.025973	-2.90319	Down	acyl-CoA oxidase 2
RASSF9	-2.41937	0.002996	0.022378	-2.96817	Down	Ras association domain family member 9
AKNA	-2.41806	2.82E-06	7.71E-05	-4.68362	Down	AT-hook transcription factor
ESAM	-2.40768	7.39E-05	0.001167	-3.96338	Down	endothelial cell adhesion molecule
FBN2	-2.40672	0.008006	0.046061	-2.65183	Down	fibrillin 2
C19orf33	-2.40386	4.52E-07	1.64E-05	-5.04584	Down	chromosome 19 open reading frame 33
LOC644656	-2.40278	0.002798	0.021326	-2.98915	Down	uncharacterized LOC644656
PCDHB5	-2.40027	0.000313	0.003872	-3.60443	Down	protocadherin beta 5
GHR	-2.39572	0.006329	0.038709	-2.73023	Down	growth hormone receptor
IGSF9	-2.39305	0.000112	0.001649	-3.86333	Down	immunoglobulin superfamily member 9
CDC6	-2.3927	0.000947	0.009363	-3.30573	Down	cell division cycle 6
ZSCAN20	-2.38179	4.74E-05	0.000817	-4.06812	Down	zinc finger and SCAN domain containing 20
TRPA1	-2.37958	3.39E-06	9.08E-05	-4.6454	Down	transient receptor potential cation channel subfamily A member 1
CERS4	-2.37699	3.01E-07	1.15E-05	-5.12261	Down	ceramide synthase 4
RGS5	-2.37518	4.56E-07	1.65E-05	-5.04413	Down	regulator of G protein signaling 5
MFAP4	-2.37381	2.11E-09	1.40E-07	-5.98924	Down	microfibril associated protein 4
SNTB1	-2.37108	1.28E-05	0.000279	-4.36296	Down	syntrophin beta 1
TGFB3	-2.37062	1.28E-10	1.15E-08	-6.42986	Down	transforming growth factor beta 3
ARAP3	-2.36298	6.30E-05	0.001029	-4.0011	Down	ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 3
DCX	-2.35488	5.92E-10	4.60E-08	-6.19261	Down	doublecortin
DOK6	-2.35163	0.001404	0.012641	-3.19388	Down	docking protein 6
REM2	-2.33807	0.000734	0.007608	-3.37667	Down	RRAD and GEM like GTPase 2
MST1R	-2.33382	0.000891	0.008939	-3.32291	Down	macrophage stimulating 1 receptor
ADCK2	-2.33367	4.19E-07	1.53E-05	-5.05994	Down	aarF domain containing kinase 2
ZNF382	-2.33358	1.08E-06	3.48E-05	-4.87723	Down	zinc finger protein 382
ITPKB	-2.33313	8.26E-05	0.001283	-3.93677	Down	inositol-trisphosphate 3-kinase B
TCF7L1	-2.32815	4.07E-06	0.000106	-4.6079	Down	transcription factor 7 like 1
COLEC11	-2.32755	0.005638	0.035504	-2.76815	Down	collectin subfamily member 11
RTEL1	-2.3271	0.002213	0.017864	-3.05999	Down	regulator of telomere elongation helicase 1
PLAU	-2.32405	4.95E-10	3.93E-08	-6.22066	Down	plasminogen activator, urokinase
ZNF225	-2.32232	1.94E-05	0.000392	-4.27161	Down	zinc finger protein 225
TEKT2	-2.32148	7.70E-05	0.001207	-3.9537	Down	tektin 2
SNORD116-20	-2.32074	0.000412	0.004825	-3.53253	Down	small nucleolar RNA, C/D box 116-20
PLXNA4	-2.31931	0.007018	0.041668	-2.69601	Down	plexin A4
LYG1	-2.31421	0.001683	0.014407	-3.14107	Down	lysozyme g1

KLRK1	-2.31205	5.92E-07	2.05E-05	-4.99391	Down	killer cell lectin like receptor K1
PPP4R1L	-2.30845	0.000193	0.002608	-3.72846	Down	protein phosphatase 4 regulatory subunit 1 like (pseudogene)
RAB36	-2.30784	1.33E-07	5.62E-06	-5.27483	Down	RAB36, member RAS oncogene family
GPRC5A	-2.30755	1.59E-07	6.56E-06	-5.24219	Down	G protein-coupled receptor class C group 5 member A
MICAL2	-2.30536	4.40E-10	3.55E-08	-6.23919	Down	microtubule associated monooxygenase, calponin and LIM domain containing 2
CNN1	-2.30412	0.006192	0.038125	-2.73741	Down	calponin 1
CABLES1	-2.28816	5.14E-05	0.000873	-4.04934	Down	Cdk5 and Abl enzyme substrate 1
HEY1	-2.28283	1.51E-06	4.69E-05	-4.80928	Down	hes related family bHLH transcription factor with YRPW motif 1
STAMBPL1	-2.2809	0.0002	0.002685	-3.71904	Down	STAM binding protein like 1
FILIP1	-2.27926	0.000297	0.003712	-3.6177	Down	filamin A interacting protein 1
TCF19	-2.27043	0.005182	0.033297	-2.79551	Down	transcription factor 19
ADM2	-2.2693	7.21E-05	0.00115	-3.96924	Down	adrenomedullin 2
F2RL3	-2.26218	0.006973	0.041522	-2.69811	Down	F2R like thrombin or trypsin receptor 3
JAK3	-2.25837	7.02E-10	5.27E-08	-6.16561	Down	Janus kinase 3
AMPD3	-2.25431	1.17E-07	5.02E-06	-5.29776	Down	adenosine monophosphate deaminase 3
LOC283922	-2.25375	0.000198	0.002659	-3.72171	Down	pyruvate dehydrogenase phosphatase regulatory subunit pseudogene
PRC1	-2.24885	0.001354	0.012271	-3.20439	Down	protein regulator of cytokinesis 1
OMD	-2.2486	0.000424	0.004948	-3.5246	Down	osteomodulin
CAPN3	-2.2486	0.000375	0.004463	-3.55721	Down	calpain 3
CENPL	-2.24563	0.000284	0.003592	-3.62991	Down	centromere protein L
AGPAT4	-2.24338	1.76E-08	9.81E-07	-5.63375	Down	1-acylglycerol-3-phosphate O-acyltransferase 4
TNFRSF9	-2.24232	0.000673	0.007129	-3.40031	Down	TNF receptor superfamily member 9
THBS2	-2.23939	1.53E-08	8.69E-07	-5.65772	Down	thrombospondin 2
GATA4	-2.23356	0.001673	0.014344	-3.14287	Down	GATA binding protein 4
ZNF578	-2.22449	5.95E-11	5.93E-09	-6.54494	Down	zinc finger protein 578
NLRP1	-2.22383	0.005604	0.035369	-2.77008	Down	NLR family pyrin domain containing 1
IFITM1	-2.22304	5.17E-12	6.34E-10	-6.90092	Down	interferon induced transmembrane protein 1
CDCA7L	-2.21912	0.000175	0.002415	-3.75311	Down	cell division cycle associated 7 like
SULF2	-2.21472	7.92E-11	7.69E-09	-6.5021	Down	sulfatase 2
MMP11	-2.21439	4.16E-06	0.000108	-4.60305	Down	matrix metallopeptidase 11
NGF	-2.2138	0.008589	0.048333	-2.62798	Down	nerve growth factor
IL1RAP	-2.2124	8.29E-09	4.96E-07	-5.76255	Down	interleukin 1 receptor accessory protein
ASPN	-2.21173	9.25E-05	0.001406	-3.90938	Down	asporin
KLHDC8B	-2.20812	4.15E-07	1.52E-05	-5.06209	Down	kelch domain containing 8B
EFNA4	-2.20663	0.008279	0.047176	-2.64048	Down	ephrin A4
CTHRC1	-2.20605	6.86E-06	0.000164	-4.49806	Down	collagen triple helix repeat containing 1
OLFM1	-2.20308	7.85E-09	4.76E-07	-5.77156	Down	olfactomedin 1
CETN4P	-2.19988	0.00501	0.032446	-2.80642	Down	centrin 4, pseudogene
NFE2L3	-2.19936	4.59E-06	0.000116	-4.58292	Down	nuclear factor, erythroid 2 like 3
KIF14	-2.19759	0.008838	0.04936	-2.61825	Down	kinesin family member 14
SNORD57	-2.19175	1.87E-05	0.000381	-4.27993	Down	small nucleolar RNA, C/D box 57
LPAR6	-2.18519	4.28E-11	4.32E-09	-6.59411	Down	lysophosphatidic acid receptor 6

PLAT	-2.18436	6.98E-09	4.28E-07	-5.79147	Down	plasminogen activator, tissue type
FUT4	-2.1843	4.79E-08	2.30E-06	-5.459	Down	fucosyltransferase 4
ANKRD36BP2	-2.18367	1.37E-09	9.50E-08	-6.0584	Down	ankyrin repeat domain 36B pseudogene 2
ZNF74	-2.18352	3.01E-06	8.17E-05	-4.66989	Down	zinc finger protein 74
TMEM204	-2.17915	0.007828	0.0452	-2.65939	Down	transmembrane protein 204
GFPT2	-2.17823	1.08E-06	3.50E-05	-4.87557	Down	glutamine-fructose-6-phosphate transaminase 2
C22orf42	-2.17509	1.42E-06	4.45E-05	-4.82203	Down	chromosome 22 open reading frame 42
NHS	-2.17259	1.37E-05	0.000297	-4.34817	Down	NHS actin remodeling regulator
EFS	-2.16928	0.004816	0.031576	-2.81908	Down	embryonal Fyn-associated substrate
ADAM19	-2.16658	1.99E-08	1.08E-06	-5.61289	Down	ADAM metallopeptidase domain 19
APOBEC3B	-2.16319	6.86E-06	0.000164	-4.49784	Down	apolipoprotein B mRNA editing enzyme catalytic subunit 3B
CHTF18	-2.16232	0.00212	0.017258	-3.07291	Down	chromosome transmission fidelity factor 18
KNDC1	-2.15888	6.74E-05	0.001089	-3.98525	Down	kinase non-catalytic C-lobe domain containing 1
CHEK1	-2.15805	1.94E-05	0.000392	-4.27124	Down	checkpoint kinase 1
MCAM	-2.15289	3.80E-07	1.41E-05	-5.07866	Down	melanoma cell adhesion molecule
LCP1	-2.15194	4.07E-05	0.000715	-4.10363	Down	lymphocyte cytosolic protein 1
LRFN5	-2.14996	0.006628	0.039915	-2.71496	Down	leucine rich repeat and fibronectin type III domain containing 5
ACSM3	-2.14536	2.20E-10	1.88E-08	-6.34645	Down	acyl-CoA synthetase medium chain family member 3
DCAF4	-2.1387	1.56E-05	0.000326	-4.32021	Down	DDB1 and CUL4 associated factor 4
MTBP	-2.13416	0.001085	0.010338	-3.2676	Down	MDM2 binding protein
KLHL1	-2.13391	0.002973	0.022264	-2.97051	Down	kelch like family member 1
VANGL1	-2.12864	1.83E-06	5.51E-05	-4.77175	Down	VANGL planar cell polarity protein 1
GPX8	-2.1259	3.62E-09	2.34E-07	-5.90058	Down	glutathione peroxidase 8 (putative)
LOC100379224	-2.12575	1.98E-06	5.82E-05	-4.7552	Down	uncharacterized LOC100379224
TIPIN	-2.1246	1.64E-05	0.000341	-4.30951	Down	TIMELESS interacting protein
SPRY4	-2.12151	2.05E-06	5.98E-05	-4.74849	Down	sprouty RTK signaling antagonist 4
PTPRE	-2.11764	7.05E-09	4.31E-07	-5.78979	Down	protein tyrosine phosphatase receptor type E
C10orf55	-2.11758	0.000531	0.005903	-3.46456	Down	chromosome 10 putative open reading frame 55
EMP1	-2.11626	1.21E-08	7.01E-07	-5.69857	Down	epithelial membrane protein 1
ZNF660	-2.11231	1.86E-06	5.57E-05	-4.76806	Down	zinc finger protein 660
H19	-2.11172	7.49E-07	2.52E-05	-4.94826	Down	H19 imprinted maternally expressed transcript
TBXA2R	-2.10662	0.008229	0.047003	-2.64251	Down	thromboxane A2 receptor
USP6	-2.10526	7.52E-06	0.000178	-4.47843	Down	ubiquitin specific peptidase 6
LAMA2	-2.10455	3.11E-05	0.000579	-4.16536	Down	laminin subunit alpha 2
LOC154761	-2.10453	9.94E-05	0.001494	-3.89211	Down	family with sequence similarity 115, member C pseudogene
HHLA2	-2.1032	0.001625	0.014049	-3.15132	Down	HERV-H LTR-associating 2
ZNF350	-2.09835	6.03E-08	2.80E-06	-5.41803	Down	zinc finger protein 350
GPR82	-2.09727	0.000466	0.005327	-3.49961	Down	G protein-coupled receptor 82
RPTOR	-2.09525	4.42E-05	0.000768	-4.08461	Down	regulatory associated protein of MTOR complex 1
PRPH2	-2.09306	2.24E-05	0.000442	-4.23918	Down	peripherin 2
SYTL2	-2.09238	9.57E-06	0.000218	-4.4266	Down	synaptotagmin like 2
ZNF577	-2.09237	5.29E-05	0.000894	-4.04223	Down	zinc finger protein 577
CHL1	-2.09068	5.84E-05	0.000967	-4.01912	Down	cell adhesion molecule L1 like

DNAJC22	-2.08584	2.39E-06	6.69E-05	-4.71712	Down	DnaJ heat shock protein family (Hsp40) member C22
SPARCL1	-2.08481	1.46E-05	0.00031	-4.3342	Down	SPARC like 1
CXCR4	-2.08402	7.59E-05	0.001192	-3.95705	Down	C-X-C motif chemokine receptor 4
EPPK1	-2.08312	5.17E-08	2.47E-06	-5.44552	Down	epiplakin 1
ATAT1	-2.07916	1.13E-07	4.85E-06	-5.30486	Down	alpha tubulin acetyltransferase 1
RYR3	-2.07755	0.00289	0.021795	-2.97916	Down	ryanodine receptor 3
PRR11	-2.07467	0.000171	0.002372	-3.7581	Down	proline rich 11
ZNF624	-2.06913	2.27E-05	0.000447	-4.23646	Down	zinc finger protein 624
ARHGAP6	-2.06665	0.004771	0.031366	-2.82207	Down	Rho GTPase activating protein 6
FAT4	-2.06599	0.000946	0.009363	-3.30624	Down	FAT atypical cadherin 4
LOC374443	-2.06089	0.00379	0.026492	-2.89513	Down	C-type lectin domain family 2 member D pseudogene
FGG	-2.05957	0.002532	0.019815	-3.01947	Down	fibrinogen gamma chain
STK10	-2.05632	4.63E-06	0.000117	-4.5811	Down	serine/threonine kinase 10
TEAD3	-2.0544	8.36E-05	0.00129	-3.93384	Down	TEA domain transcription factor 3
ZNF778	-2.05438	0.006697	0.040233	-2.71153	Down	zinc finger protein 778
ZNF564	-2.052	1.00E-07	4.41E-06	-5.32623	Down	zinc finger protein 564
FAM200A	-2.05146	1.68E-06	5.12E-05	-4.7889	Down	family with sequence similarity 200 member A
IGF2	-2.05109	6.07E-14	9.69E-12	-7.50655	Down	insulin like growth factor 2
BACH2	-2.05081	1.83E-06	5.51E-05	-4.77135	Down	BTB domain and CNC homolog 2
LRRC37B	-2.0495	9.93E-08	4.38E-06	-5.32793	Down	leucine rich repeat containing 37B
NOX5	-2.04697	0.003455	0.024799	-2.92404	Down	NADPH oxidase 5
DDR2	-2.04377	4.94E-07	1.77E-05	-5.02879	Down	discoidin domain receptor tyrosine kinase 2
FOXQ1	-2.04319	0.000588	0.006397	-3.43689	Down	forkhead box Q1
TMEM116	-2.04083	3.23E-08	1.66E-06	-5.52823	Down	transmembrane protein 116
RNF138P1	-2.03873	1.47E-05	0.00031	-4.33385	Down	ring finger protein 138 pseudogene 1
MEX3A	-2.03718	0.000573	0.006263	-3.4442	Down	mex-3 RNA binding family member A
SEMA3A	-2.03545	9.14E-05	0.001393	-3.91241	Down	semaphorin 3A
ZNF300P1	-2.03197	0.002385	0.018952	-3.03753	Down	zinc finger protein 300 pseudogene 1
NAA40	-2.0275	1.04E-09	7.43E-08	-6.10309	Down	N-alpha-acetyltransferase 40, NatD catalytic subunit
DAND5	-2.02131	0.000699	0.00735	-3.38988	Down	DAN domain BMP antagonist family member 5
TFF1	-2.0112	0.004679	0.030977	-2.82835	Down	trefoil factor 1
NOTCH3	-2.00738	2.63E-08	1.38E-06	-5.56445	Down	notch receptor 3
RRN3P2	-2.00495	2.82E-05	0.000538	-4.18763	Down	RRN3 pseudogene 2
RFTN1	-2.00494	0.006985	0.041558	-2.69758	Down	raftlin, lipid raft linker 1
USH2A	-2.00478	0.00357	0.025308	-2.91384	Down	usherin
HPSE	-2.00475	0.003458	0.024806	-2.92381	Down	heparanase
NKAPL	-2.00325	1.27E-05	0.000277	-4.3652	Down	NFKB activating protein like
DGKD	-2.00014	3.76E-09	2.42E-07	-5.89422	Down	diacylglycerol kinase delta
ARHGAP31	-1.9977	0.000157	0.002214	-3.77925	Down	Rho GTPase activating protein 31
ZNF565	-1.99447	0.001321	0.012061	-3.21146	Down	zinc finger protein 565
C2orf88	-1.99129	0.000208	0.002777	-3.70889	Down	chromosome 2 open reading frame 88

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

GO ID	CATEGORY	GO Name	P Value	FDR B&H	FDR B&Y	Bonferroni	Gene Count	Gene
				Up regulated genes				
GO:0006952	BP	defense response	3.72E-10	2.20E-06	2.03E-05	2.20E-06	84	HIF1A,HLA-A,HLA-B,HLA-C,HLA-DPB1,HLA-DRA,HLA-DRB1,PENK,HLA-E,HLA-F,HLA-H,TUSC2,CHI3L1,ADORA2A,SAA1,SAA2,SERPINA1,ADRB2,CLU,AGT,FGA,CCL20,HSPA1B,VCAM1,MUC20,DUOXA2,MRC1,ZC3H12A,UBD,MUC15,APCS,BIRC3,DUOX2,IFITM2,PPARA,MUC13,SUCNR1,APOL1,RAB20,CRH,ZFP36,PPM1B,CRP,PLA2G4C,DUOXA1,SLPI,SOCS1,SNCA,CYP4F11,ABHD12,CTSS,IL6R,DAB2IP,SPP1,GBP2,ITGAX,GRAMD4,CFB,DEFB1,JUN,VNN1,KCNJ8,SERPING1,C1R,C4BPA,KLKB1,KYNU,RAB27A,NR1H4,DPP4,RARRES2,GPX2,CASP1,RELA,LCN2,CXCL2,LDLR,ORM1,GSDMD,REG3A,CD74,RORA,CD81,LYZ
GO:0046903	BP	secretion	3.05E-09	3.40E-06	3.15E-05	1.80E-05	81	ERBB3,HIF1A,HLA-E,HLA-F,HLA-H,PFKL,CHI3L1,TTR,LRG1,ADORA2A,SAA1,SERPINA1,SERPINE2,ADRB1,ADRB2,PIGR,CLU,AGT,FGA,ALB,C1QTNF4,HSPA1B,SDC4,DPP7,ZC3H12A,ANG,LAT2,ANXA4,SUCNR1,APOH,IDUA,CRH,CRP,MMRN1,CARTPT,PIM3,STX19,ARSA,PPY,STXBP6,SLPI,FTH1,SOCS1,SNCA,CTSD,CTSS,PRLR,GAA,GABBR1,SPP1,CPLX2,GCG,ITGAX,PGRMC1,QSOX1,KCNC4,PTPRN2,VNN1,CYB5R3,SERPING1,KCNQ1,CACNA1H,RAB27A,NR1H4,RAB5C,CA2,CACNA1A,DPP4,RAP1A,RARRES2,FFAR1,CASP1,NR4A3,LCN2,SLC44A4,ATP13A2,O

								RM1,GSDMD,CD74,TNFAIP2,LYZ
GO:0099503	CC	secretory vesicle	1.46E-07	8.06E-06	5.73E-05	9.94E-05	52	PCSK2,PENK,HLA-H,CHGB,PFKL,CHI3L1,TTR,LRG1,SERPINA1,SERPINE2,PIGR,CLU,SCNN1A,FGA,ALB,HSPA1B,DPP7,CLIP2,APOH,MMRN1,CARTPT,STX19,ARSA,SLPI,FTH1,SNCA,CTSD,CTSS,GAA,GABBR1,GCG,ITGAX,PGRMC1,QSOX1,KCNC4,PTPRN2,VNN1,CYB5R3,SERPING1,KCNQ1,PCSK1N,RAB27A,RAB5C,CA4,RAP1A,ROGDI,RARRES2,LCN2,ORM1,RNPEP,GSDMD,LYZ
GO:0005794	CC	Golgi apparatus	9.60E-06	2.85E-04	2.03E-03	6.56E-03	64	MAN1A1,GCNT3,HLA-A,HLA-B,HLA-C,BET1,HLA-DPB1,HLA-DRA,TRAPPC5,HLA-DRB1,DAPK2,HLA-E,HLA-F,HLA-H,PLEKHB1,RTN1,F10,ABCB1,ADORA2A,SERPINA1,RAB33A,CLU,SEC24B,DDX54,ALB,SDC4,VCAM1,MUC20,DPP7,MUC15,ST8SIA1,MUC13,RAB20,GBA2,STS,PSMG1,CERS1,SNCA,FAM20A,GGA1,TMEM30B,GGA2,GALNT3,SPP1,GBP2,GNPTG,DEFB1,QSOX1,KCNC4,DHCR24,PCSK1N,RAB27A,CA4,DPP4,RAP1GAP,SCYL3,NUCB1,STEAP4,OCRL,GRINA,LDLR,RNPEP,CD74,KLHL12
GO:0042802	MF	identical protein binding	7.07E-06	9.36E-04	7.17E-03	8.43E-03	77	ERBB3,CEBPD,ZBTB48,MAT1A,DAPK2,PEX7,OIP5,PFKL,NR4A1,PLEKHB1,TTR,F11,PGR,ADH1C,ADORA2A,SERPINA1,ADRB2,PLIN5,MAP3K9,ALB,ALDH2,ALDOB,SDC4,MOCS2,AMBP,NECAB2,ANG,ANXA4,AOX1,APCS,PON3,CLDN7,MUC13,APOH,CRP,ASL,FTH1,SNCA,SLC4A4,PRLR,IL6R,MVD,SOD2,DAB2IP,IMPA2,GAMT,GBP2,LHPP,GCG,S100Z,GNPTG,DEFB1,RASSF5,JUN,

								KCNQ1,KYNU,DPP4,RAP1GAP,NUDT16,NR4A2,CASP1,NR4A3,RELA,LCN2,TYMP,LDLR,TFRC,MLXIPL,CDH22,RPRD1A,P4HA1,REG3A,CD74,KLHL12,LYZ,CDH17,MAF
GO:0022857	MF	transmembrane transporter activity	7.16E-04	2.84E-02	2.18E-01	8.53E-01	50	PDE4D,SLC24A3,SLC22A17,CHRNE,ABCB1,KCNH6,ADRB1,ADRB2,COX5A,SCN3A,SCNN1A,CNGA1,AMBP,HCN3,SLC34A2,APOL1,CRH,SHANK2,SLC17A1,SLCO1A2,SLC6A20,C15orf48,SNCA,SLC4A4,SLC12A7,CTSS,CACNA2D3,GABRE,CHCHD10,SLC39A1,SLC28A3,GC,KCNC4,KCNJ8,SLMAP,KCNK3,KCNQ1,CACNA1H,SLC29A4,CACNA1A,SLC38A4,SLC19A3,SLC44A4,ATP13A2,TFRC,SLC25A36,TMC5,SLC25A19,SLC16A7,CDH17
Down regulated genes								
GO:0007155	BP	cell adhesion	9.22E-24	1.36E-20	1.26E-19	5.42E-20	101	EPHB6,PDGFRA,EFS,PECAM1,MCAM,PCDH12,ADA,MFAP4,MFGE8,BTN2A2,FBN1,MYL9,LRFN5,COL14A1,IGSF9,PLAU,SPARCL1,SRPX,FGG,PCDH18,COL1A1,COL3A1,COL5A1,NID2,COL6A2,COL6A3,ITGA11,COL12A1,COL15A1,FN1,ABI3BP,FAT3,MXRA8,COL5A3,ARG1,KLRK1,CD93,POSTN,ARHGAP6,IGF2,VCAN,SNAI2,CNTNAP2,PLXNA4,DCHS1,IL1RAP,MUC4,NEXN,CHL1,IL18,ADAM19,PCDHB5,LAMA1,ISLR,HPSE,ITPKB,PTN,JAK3,STK10,BMP4,NTNG2,SRPX2,CLEC4A,CXCR4,NTM,GLI2,KIF14,NID1,KDR,KIT,UNC5D,FAT4,KIF26B,ECM2,DDR2,AKNA,LAMA2,LAMA4,ESAM,PRPH2,OMD,S1PR1,ADAMTS12,TGFBI,HHLA2,THBS1,THBS2,EFNB2,THY1,CD34,SERPINE1,MMRN2,TNFAIP6,HAS2,LE

								F1,CDH5,PCDH7,CDH6,CDH11,FRMD5,CDH13
GO:0051674	BP	localization of cell	1.21E-15	4.46E-13	4.13E-12	7.14E-12	100	SYNPO2,ERG,PDGFB,PDGFRA,EFS,PECAM1,ACTA2,MCAM,SOX18,ADA,F2R,PGF,SEMA3A,WNT5B,ADORA2B,ANLN,ASPM,HRH1,CTHRC1,OLFM1,PLAT,PLAU,MMP9,RSPH9,COL1A1,COL1A2,COL3A1,COL5A1,SEMA3C,ITGA11,FN1,DLL4,FAT3,IFITM1,KLRK1,POSTN,IGF2,VCAN,SNAI2,PLXNA4,DCHS1,GLIPR2,NRG3,NEXN,SIX2,CHL1,IL16,SPARC,IL18,EPPK1,LAMA1,TUBB2B,SST,DCX,PTGS2,PTN,STK10,BMP4,TEKT2,SRPX2,GPC3,CXCR4,SULF1,KIF14,KDR,KIT,UNC5D,TBXA2R,TMSB15A,RIPK3,CD248,FFAR2,DDR2,LAMA2,LAMA4,ESAM,LCP1,ECM1,S1PR1,EDNRA,ADAMTS12,THBS1,ARAP3,EFNB2,EGF,THY1,LOX,CD34,SERPINE1,MMRN2,SLC7A5,CDK1,TNFAIP6,HAS2,LEF1,PADI2,CDH5,ENPEP,FRMD5,CDH13
GO:0031012	CC	extracellular matrix	1.31E-36	7.24E-34	5.00E-33	7.24E-34	77	A2M,PDGFB,COL22A1,COLQ,WNT5B,MFAP2,MFAP4,MFGE8,FBN1,FBN2,MGP,AEBP1,CTHRC1,COL14A1,PLAT,SPARCL1,SRPX,MMP3,FGG,MMP9,MMP11,USH2A,COL1A1,COL1A2,COL3A1,COL4A1,COL5A1,COL5A2,NID2,COL6A2,COL6A3,SEMA3C,COL12A1,COL15A1,FN1,ABI3BP,ADAMTS2,OLFML2B,COL5A3,POSTN,IGF2,VCAN,MUC4,IL16,SPARC,ADAM19,ASPN,LAMA1,HPSE,BGN,PTN,SRPX2,PXDN,GPC3,SULF1,NID1,INHBE,CD248,ECM2,LAMA2,LAMA4,OMD,ECM1,TNFRSF11B,TGFB3,TGFBI,THBS1,THBS2,TIMP3,LOX,SERPINE1,MMRN2,IL1RL1,LTBP2,LUM,CDH13,LRRC17

GO:0031226	CC	intrinsic component of plasma membrane	6.42E-07	2.97E-05	2.05E-04	3.56E-04	72	EPHB6,KCNH7,PDGFRA,PCDH12,F2R,SEMA3A,ADORA2B,LRFN5,UPK1B,HRH1,OLFM1,ECEL1,MME,LTB4R,ALK,PCDH18,LRRC8E,SEMA3C,ITGA11,DLL4,SGCD,TMPRSS11E,SLC1A3,SLC2A2,IGDCC4,KLRK1,MST1R,SLCO2A1,SLC22A3,CNTNAP2,PLXNA4,ULBP1,NRG3,IL1RAP,MUC4,SLC16A10,TNFRSF9,NOX5,PCDHB5,LRRC70,GGT5,GHR,GJA4,NTNG2,GPC3,CLEC4A,GLRA1,TMEM150C,KDR,STRA6,KIT,NOTCH3,TBXA2R,TRPA1,F2RL3,FFAR2,DDR2,ANO1,PRPH2,GPRC5A,S1PR1,S1PR3,EDNRA,EFNA4,EFNB2,THY1,LPAR6,CD34,CALCRL,HAS2,PCDH7,ENPEP
GO:0005198	MF	structural molecule activity	1.52E-13	4.81E-11	3.58E-10	1.44E-10	55	COL22A1,COLQ,MFAP2,MFAP4,MFGE8,FBN1,FBN2,MYL9,MGP,AEBP1,UPK1B,CTHRC1,COL14A1,SRPX,FGG,COL1A1,COL1A2,COL3A1,COL4A1,COL5A1,COL5A2,NID2,COL6A2,COL6A3,COL12A1,COL15A1,FN1,ABI3BP,COL5A3,POSTN,VCAN,MUC4,NEXN,SNTB1,SPARC,EPPK1,ASPN,LAMA1,TUBB2B,BGN,SRPX2,PXDN,NID1,KRT6B,KRT17,CAPN3,LAMA2,LAMA4,ECM1,TGFBI,THBS1,THBS2,MMRN2,LTBP2,LUM

Biological Process(BP), Cellular Component(CC) and Molecular Functions (MF)

Table 4 The enriched pathway terms of the up and down regulated differentially expressed genes

Pathway ID	Pathway Name	P-value	FDR B&H	FDR B&Y	Bonferroni	Gene Count	Gene
			Up regulated genes				
1457780	Neutrophil degranulation	6.39E-06	1.26E-03	9.10E-03	5.03E-03	31	HLA-A,HLA-B,HLA-C,HLA-H,PFKL,CHI3L1,TTR,LRG1,SERPINA1,PIGR,HSPA1B,DPP7,ARSA,SLP

							I,FTH1,CTSD,CTSS,GAA,ITGAX,PGRMC1,QSOX1,PTPRN2,VNN1,CYB5R3,RAB27A,RAB5C,RAP1A,LCN2,ORM1,GSDMD,LYZ
1269203	Innate Immune System	9.95E-05	1.31E-02	9.45E-02	7.83E-02	57	ERBB3,HLA-A,HLA-B,HLA-C,HLA-E,HLA-H,PFKL,CHI3L1,NR4A1,TTR,LRG1,SAA1,SERPINA1,PIGR,CLU,FGA,HSPA1B,KLB,MUC20,DPP7,LAT2,MUC15,BIRC3,MUC13,CRP,ARSA,SLPI,FTH1,SOCS1,CTSD,CTSS,GAA,DAB2IP,ITGAX,PGRMC1,CFB,DEFB1,QSOX1,JUN,PTPRN2,VNN1,CYB5R3,C1R,C4BPA,RAB27A,RAB5C,RAP1A,DUSP1,DUSP8,CASP1,CASP10,RELA,LCN2,ORM1,GSDMD,REG3A,LYZ
1269310	Cytokine Signaling in Immune system	9.77E-04	5.91E-02	4.28E-01	7.69E-01	35	ERBB3,HIF1A,CEBPD,HLA-A,HLA-B,HLA-C,HLA-DPB1,HLA-DRA,HLA-DRB1,HLA-E,HLA-F,HLA-H,SAA1,FGA,MMP1,CCL20,VCAM1,KLB,BIRC3,IFITM2,PPM1B,SOCS1,PRLR,IL6R,DAB2IP,GBP2,ITGAX,RAP1A,DUSP1,DUSP8,CASP1,RELA,LCN2,CXCL2,RORA
1270144	Metabolism of vitamins and cofactors	2.57E-03	1.36E-01	9.83E-01	1.00E+00	12	TTR,SDC4,MOCS2,PNLIP,AOX1,GC,VNN2,VNN1,CYB5R3,SLC19A3,LDLR,SLC25A19
1269367	Platelet degranulation	2.59E-03	1.36E-01	9.83E-01	1.00E+00	10	SERPINA1,CLU,FGA,ALB,APOH,MMRN1,QSOX1,SERPING1,RARRES2,ORM1
1269907	SLC-mediated transmembrane transport	9.26E-03	2.80E-01	1.00E+00	1.00E+00	15	SLC24A3,ALB,SLC34A2,CP,SLC17A1,SLCO1A2,SLC6A20,SLC4A4,SLC12A7,SLC39A1,SLC28A3,SLC29A4,SLC38A4,SLC44A4,SLC16A7
			Down regulated genes				
1270244	Extracellular matrix	2.05E-25	1.40E-22	9.91E-22	1.40E-22	49	A2M,PDGFB,PECAM1,COL22A1,MFAP2,MFAP4,FBN1,FBN2,COL14A

	organization						1,MMP3,FGG,MMP9,MMP11,COL1A1,COL1A2,COL3A1,COL4A1,COL5A1,COL5A2,NID2,COL6A2,COL6A3,ITGA11,COL12A1,COL15A1,FN1,ADAMTS2,COL5A3,VCAN,CTSK,SPARC,ASPN,LAMA1,P4HA3,BGN,BMP4,ADAMTS16,NID1,KDR,CAPN3,DDR2,LAMA2,LAMA4,TGFB3,THBS1,LOX,SERPINE1,LTBP2,LUM
1269010	Diseases of glycosylation	3.76E-07	4.27E-05	3.03E-04	2.56E-04	13	ADAMTS2,VCAN,MUC4,BGN,GPC3,ADAMTS16,NOTCH3,OMD,ADAMTS12,THBS1,THBS2,ADAMTS6,LUM
1269350	Platelet activation, signaling and aggregation	5.91E-06	4.03E-04	2.86E-03	4.03E-03	22	A2M,PDGFB,PECAM1,F2R,FGG,FN1,DGKD,IGF2,CSF2,SPARC,ISLR,JAK3,TBXA2R,F2RL3,ECM1,TGFB3,THBS1,EGF,TIMP3,SERPINE1,DGKI,PCDH7
1269340	Hemostasis	8.35E-05	4.29E-03	3.05E-02	5.69E-02	34	A2M,PDGFB,CENPE,PECAM1,F2R,PLAT,PLAU,FGG,KIF6,FN1,DGKD,IGF2,CSF2,SPARC,GATA4,ISLR,CABLES1,JAK3,KIF2C,TBXA2R,F2RL3,KIF26B,ESAM,ECM1,TGFB3,THBS1,EGF,GUCY1A2,TIMP3,SERPINE1,DGKI,SLC7A5,PCDH7,SERPIND1
1270303	Axon guidance	1.66E-03	4.51E-02	3.20E-01	1.00E+00	27	EPHB6,DOK6,PDGFB,PDGFRA,SEMA3A,MYL9,FGG,MMP9,COL4A1,COL6A2,COL6A3,FN1,CSF2,PLXNA4,NRG3,CHL1,GAP43,LAMA1,DCX,JAK3,KDR,ST8SIA4,KIT,UNC5D,EFNA4,EFNB2,EGF
1269592	Gastrin-CREB signalling pathway via PKC and MAPK	7.76E-03	1.82E-01	1.00E+00	1.00E+00	21	PDGFB,PDGFRA,F2R,HRH1,LTB4R,MMP3,FGG,FN1,DGKD,CSF2,NRG3,GHRL,JAK3,KIT,TBXA2R,F2RL3,FFAR2,EDNRA,EGF,LPAR6,DGKI

Table 5 Topology table for up and down regulated genes

Regulation	Node	Degree	Betweenness	Stress	Closeness
Up	JUN	1596	0.297948	5.04E+08	0.437877
Up	VCAM1	661	0.055649	1.83E+08	0.379038
Up	RELA	440	0.066286	65857496	0.392096
Up	U2AF2	401	0.032981	50615222	0.375241
Up	ADRB2	360	0.051656	1.09E+08	0.357594
Up	PPP1CC	350	0.055551	48521756	0.382627
Up	POLR2A	320	0.042098	73677082	0.357008
Up	CD81	244	0.02104	53426396	0.344262
Up	SDHA	228	0.023854	17009994	0.380039
Up	SNCA	224	0.025545	56250412	0.341272
Up	ALB	217	0.032126	27109520	0.350929
Up	ERBB3	207	0.023464	46497836	0.338957
Up	HIF1A	201	0.022327	16543606	0.372868
Up	OCRL	183	0.021433	38355000	0.33816
Up	MRPL12	182	0.021656	24757490	0.335917
Up	RAB5C	164	0.019293	18077018	0.349243
Up	CCDC85B	148	0.026064	17688698	0.320629
Up	CLU	148	0.018422	34351976	0.331337
Up	FTH1	112	0.015754	15114778	0.329531
Up	TFRC	110	0.016321	10628564	0.378798
Up	SPINT2	108	0.018333	13787598	0.314599
Up	MRPL38	108	0.014795	7135306	0.347488
Up	CACNA1A	101	0.013778	14792904	0.318909
Up	SPP1	100	0.011753	13635028	0.324872
Up	GNAI1	100	0.016452	7052876	0.346084
Up	PPM1B	99	0.010628	13845334	0.333148
Up	CHN2	94	0.003043	7480904	0.324097
Up	ZBTB48	91	0.007794	14008360	0.306699

Up	ID2	88	0.008382	20399246	0.31338
Up	DUT	85	0.006791	9371824	0.325667
Up	PGR	83	0.005038	6050756	0.33088
Up	TMEM30B	80	0.012048	8252762	0.301821
Up	HSPA1B	78	0.00697	6310746	0.350331
Up	SOD2	77	0.006883	13105960	0.314833
Up	CASP1	75	0.008457	14148852	0.309164
Up	STAMBP	73	0.008256	8962166	0.315013
Up	NECAB2	72	0.00898	20828314	0.294
Up	SOCS1	71	0.00732	4459136	0.332855
Up	ATP13A2	70	0.01148	8100584	0.311952
Up	CENPB	69	0.00962	5877652	0.328913
Up	COX5A	68	0.004787	9014728	0.310793
Up	PGRMC1	67	0.005965	5851738	0.324374
Up	PFKL	67	0.005301	4220404	0.339501
Up	ZFP36	65	0.005869	5840334	0.325814
Up	SLMAP	64	0.008847	14906016	0.300925
Up	KLHL12	62	0.006002	9477918	0.31082
Up	SERPINA1	61	0.004959	3442108	0.32758
Up	CRP	61	0.00901	3976752	0.320944
Up	HLA-DRA	58	0.006376	6984242	0.303374
Up	SEC24B	57	0.005122	7921100	0.311736
Up	HLA-E	57	0.008193	5417646	0.301114
Up	RASSF5	54	0.005973	5581726	0.309603
Up	CYB5R3	53	0.005535	4457008	0.322007
Up	DUSP1	50	0.0047	10162126	0.297576
Up	LYZ	48	0.004406	2822858	0.352771
Up	DTNB	46	0.006085	5998870	0.297047
Up	GBP2	46	0.002674	2254472	0.315954
Up	KYNU	45	0.003541	8318140	0.294385

Up	ZBTB7A	44	0.003479	2378948	0.318641
Up	NUCB1	44	0.003535	3000438	0.311156
Up	GABRE	42	0.006362	6963592	0.273467
Up	DUSP8	42	0.003924	3730912	0.305695
Up	FGA	41	0.002177	1408648	0.322498
Up	VNN2	39	0.004648	4918216	0.275309
Up	PIGR	38	0.003219	4218970	0.283356
Up	CHGB	37	0.002356	1883312	0.310458
Up	HLA-DPB1	37	0.005437	4024006	0.28368
Up	MVD	37	0.00277	1785902	0.307209
Up	GPAA1	36	0.006228	5917528	0.291675
Up	POLD2	36	0.004619	5556090	0.301063
Up	DPP4	34	0.004172	1947850	0.298874
Up	RFX1	32	0.003758	7609514	0.295413
Up	EPHX1	31	0.00324	3148816	0.29602
Up	ALDOB	31	0.002792	2018518	0.30784
Up	AGT	31	0.002966	1865644	0.306294
Up	PEX7	28	0.002627	7979132	0.279546
Up	MMP1	28	0.001636	962486	0.318768
Up	IL6R	28	0.004718	1522490	0.295316
Up	AK1	27	0.002177	3763326	0.290274
Up	KCNC4	27	0.002966	4065280	0.287685
Up	MAF	26	0.001371	928624	0.315427
Up	LCN2	26	0.002077	4747150	0.281902
Up	TRIB2	26	0.002374	1372656	0.307157
Up	RNF149	26	0.003073	2741500	0.27934
Up	GC	25	0.001091	1093748	0.300309
Up	BTG1	25	0.0019	963086	0.321863
Up	KCNJ8	24	0.002693	1543874	0.254755
Up	STS	23	0.002783	1476396	0.279026

Up	CCDC86	23	7.45E-04	1261094	0.295801
Up	UBD	22	0.001864	3627404	0.290415
Up	APOH	22	9.68E-04	1240028	0.29797
Up	ABCB1	22	0.001386	2114132	0.29802
Up	RCAN2	22	0.002346	3980546	0.273
Up	DEPTOR	22	0.001221	937788	0.307538
Up	BTG2	20	6.52E-04	1046918	0.283703
Up	ARVCF	19	0.002101	909702	0.281471
Up	AMBP	17	7.00E-04	525586	0.31932
Up	CXCL2	17	9.45E-04	498648	0.305228
Up	MMRN1	17	4.60E-04	617814	0.267011
Up	FAM193B	17	0.001148	1447216	0.291699
Up	HLA-B	16	0.001753	1709356	0.316705
Up	GCG	16	0.001734	1201492	0.270831
Up	ANG	15	0.001061	1182188	0.286699
Up	RIPPLY2	13	6.72E-04	1051108	0.249022
Up	CDKN2A	11	7.57E-04	1062712	0.32113
Up	PDK4	11	5.73E-04	839962	0.257952
Up	PENK	10	0.001694	1717524	0.24922
Up	MAN1A1	10	3.87E-04	238680	0.259994
Up	GAMT	9	3.76E-04	408938	0.279872
Up	CYP3A5	8	0.001126	1514978	0.241538
Up	AOX1	8	2.93E-04	399780	0.258536
Up	HLA-DRB1	7	1.24E-04	74760	0.250776
Up	HLA-A	7	7.84E-04	861244	0.28934
Up	RAB33A	7	5.82E-04	1629132	0.221958
Up	LONP1	6	5.55E-04	2034278	0.328373
Up	HLA-H	6	1.96E-04	63810	0.271086
Up	MAP3K9	6	2.80E-04	523732	0.268857
Up	ALDH2	5	2.38E-04	448744	0.310928

Up	HLA-C	5	4.48E-04	299492	0.271342
Up	NR4A1	5	1.74E-04	265578	0.298378
Up	CARTPT	5	3.33E-04	343864	0.26055
Up	APOL1	4	1.94E-05	34026	0.25131
Up	TBL2	4	7.27E-04	1174624	0.311925
Up	TTR	4	5.60E-04	453308	0.270913
Up	CD74	4	2.05E-04	127222	0.259189
Up	CPM	4	5.33E-04	590954	0.28459
Up	TMEM176A	4	2.82E-04	303148	0.244104
Up	HAO1	4	3.12E-04	1039252	0.250113
Up	CHCHD10	3	4.87E-05	78354	0.27908
Up	SUCLG2	3	8.47E-05	93604	0.283569
Up	CTSD	3	4.02E-05	270406	0.307314
Up	DDX54	3	6.87E-05	270908	0.307341
Up	ANP32A	3	2.05E-05	65462	0.310753
Up	BIRC3	3	5.17E-05	155646	0.286608
Up	GIGYF1	2	5.44E-06	14190	0.272638
Up	RTN1	2	1.68E-05	23170	0.266921
Up	SERPING1	2	2.26E-05	9370	0.261051
Up	SERPINE2	2	2.62E-06	672	0.246784
Up	TRAPPC5	2	6.26E-05	68134	0.249861
Up	APCS	2	0	0	0.295158
Up	SERPINA6	2	3.33E-04	309232	0.296276
Up	REG3A	2	1.52E-05	52952	0.299908
Up	BBC3	2	0	0	0.259778
Up	RPRD1A	2	3.92E-05	277120	0.309669
Up	DACH1	2	0	0	0.309936
Up	RGS4	2	5.44E-05	21664	0.272307
Up	CASP10	2	3.66E-05	73078	0.264702
Up	PPARA	2	3.08E-05	28360	0.285403

Up	DHCR24	2	2.06E-05	30004	0.275109
Up	RAP1A	2	3.50E-05	22882	0.262835
Up	PCDH10	2	6.75E-06	11790	0.233911
Up	F10	2	2.24E-06	2690	0.247787
Up	PSMG1	2	0	0	0.29646
Up	CFB	2	0	0	0.297072
Up	PPP1R12B	2	1.19E-05	11496	0.250122
Up	ABLIM1	2	4.21E-05	35910	0.250479
Up	LTBP3	1	0	0	0.241806
Up	NAT9	1	0	0	0.267189
Up	GGA1	1	0	0	0.229025
Up	PJA1	1	0	0	0.239559
Up	SERPINA10	1	0	0	0.240834
Up	RNF32	1	0	0	0.249376
Up	HLA-DMB	1	0	0	0.232768
Up	SAA1	1	0	0	0.241757
Up	C4BPA	1	0	0	0.294264
Up	GABBR1	1	0	0	0.259778
Up	GET4	1	0	0	0.239455
Up	MUC20	1	0	0	0.235388
Up	NUDT16	1	0	0	0.304543
Up	ITPK1	1	0	0	0.304543
Up	FIGNL1	1	0	0	0.304543
Up	SLC25A19	1	0	0	0.304543
Up	RAP1GAP	1	0	0	0.282411
Up	RPS6KA6	1	0	0	0.247514
Up	ARRDC4	1	0	0	0.263412
Up	RAB27A	1	0	0	0.263412
Up	SPOCK3	1	0	0	0.236807
Up	DENND2D	1	0	0	0.25945

Up	FAM20A	1	0	0	0.245219
Up	TXNDC11	1	0	0	0.248884
Up	CCL20	1	0	0	0.219681
Up	HLA-F	1	0	0	0.231435
Up	LRRC24	1	0	0	0.231435
Up	BCS1L	1	0	0	0.274867
Up	MACROD1	1	0	0	0.274867
Up	KDM1B	1	0	0	0.237111
Up	WFDC2	1	0	0	0.24227
Up	SLC25A36	1	0	0	0.24227
Up	PTPRH	1	0	0	0.253159
Up	ELL	1	0	0	0.263094
Up	XAB2	1	0	0	0.263094
Up	MTMR12	1	0	0	0.229339
Up	PPP1R1B	1	0	0	0.27675
Up	POLD3	1	0	0	0.231405
Up	LSM6	1	0	0	0.231405
Up	MUC13	1	0	0	0.258853
Up	C1orf122	1	0	0	0.25146
Up	SLC22A17	1	0	0	0.219916
Up	NR1H4	1	0	0	0.28167
Up	ITGB3BP	1	0	0	0.28167
Up	PTPRN2	1	0	0	0.245663
Up	ZC3H12A	1	0	0	0.271608
Up	TMEM143	1	0	0	0.231853
Up	FAM8A1	1	0	0	0.237785
Up	QSOX1	1	0	0	0.242974
Up	LDLR	1	0	0	0.229574
Up	LRG1	1	0	0	0.294264
Up	ORM1	1	0	0	0.259778

Up	CA2	1	0	0	0.304543
Up	OIP5	1	0	0	0.304543
Up	IMPA2	1	0	0	0.245671
Up	SDC4	1	0	0	0.252041
Up	GCNT3	1	0	0	0.252041
Up	MT1A	1	0	0	0.257113
Up	FFAR1	1	0	0	0.257113
Up	CEBPD	1	0	0	0.28167
Up	CA12	1	0	0	0.231853
Up	ADORA2A	1	0	0	0.22721
Up	DOCK8	1	0	0	0.257888
Up	STX19	1	0	0	0.230169
Up	TRIOBP	1	0	0	0.242237
Up	CACNA1H	1	0	0	0.220929
Up	SLC39A1	1	0	0	0.239591
Up	P4HA1	1	0	0	0.234338
Down	FN1	800	0.121948	1.77E+08	0.416937
Down	CDK1	321	0.052371	37130306	0.393533
Down	TK1	183	0.028359	22061908	0.356407
Down	A2M	165	0.021657	31093610	0.33221
Down	ACTA2	156	0.021508	16177182	0.356813
Down	ANLN	147	0.012288	32652030	0.31966
Down	RPTOR	138	0.015393	20848032	0.33123
Down	FLNC	130	0.020359	9885742	0.364849
Down	MME	124	0.01613	22827922	0.327014
Down	CHEK1	123	0.0138	9428096	0.36459
Down	MCM6	119	0.012797	10240308	0.34408
Down	HEY1	115	0.007467	26394370	0.324521
Down	TOP2A	113	0.00822	7037480	0.366131
Down	PTN	109	0.01344	17516900	0.319717

Down	RIPK3	109	0.005618	13238646	0.329395
Down	KIT	105	0.00936	8415988	0.318274
Down	BUB1	102	0.012926	9378750	0.327669
Down	IGF2BP3	101	0.006201	5000402	0.358021
Down	CDH5	97	0.014275	14697350	0.31753
Down	STIL	94	0.010914	12929196	0.315912
Down	JAK3	93	0.006847	6645686	0.330743
Down	TUBB2B	89	0.011127	6631350	0.358521
Down	CXCR4	82	0.010003	6983362	0.336956
Down	ALK	79	0.006945	9288848	0.319235
Down	COL1A1	78	0.007539	4482218	0.336184
Down	KIF2C	78	0.00852	6501484	0.336909
Down	NOTCH3	78	0.010163	11236576	0.315068
Down	CDC6	74	0.00694	5538892	0.323892
Down	UBE2C	69	0.00668	5381164	0.318429
Down	ST8SIA4	68	0.011163	8424288	0.30563
Down	EPPK1	68	0.004854	7870332	0.320301
Down	NES	63	0.005965	5426230	0.324301
Down	GRIP1	61	0.006138	14613812	0.304595
Down	LEF1	60	0.005343	4927416	0.310793
Down	MMP9	60	0.006943	5669948	0.345071
Down	THBS1	57	0.003128	2389380	0.326747
Down	COL1A2	48	0.003029	1783500	0.32932
Down	TPX2	46	0.003701	1798214	0.340352
Down	KRT17	45	0.003227	3063576	0.325652
Down	CENPE	43	0.003357	2673372	0.310807
Down	TRIM9	43	0.004332	4076190	0.298973
Down	PLAT	42	0.004548	2384326	0.317222
Down	NEXN	40	0.002111	1827254	0.320901
Down	ARG1	39	0.003041	4412562	0.305942

Down	PTGS2	39	0.002083	2565408	0.316649
Down	PCDH7	38	0.004648	3503260	0.300108
Down	TFF1	38	0.002965	1245772	0.334139
Down	FGG	37	0.002101	1367870	0.309656
Down	HMGA2	36	9.38E-04	969146	0.320587
Down	LCP1	35	0.002865	1240328	0.343735
Down	COL5A1	34	0.001354	878512	0.318627
Down	MMP3	34	0.002251	1415208	0.31027
Down	ASB9	34	0.001201	3273876	0.29823
Down	COL6A2	33	0.003726	2359320	0.308699
Down	IL16	33	0.003152	1947338	0.313625
Down	PRC1	32	0.002506	1394808	0.310378
Down	SPARC	32	0.00126	838072	0.31898
Down	NETO2	32	0.003703	1704326	0.304298
Down	LOX	32	0.001666	910394	0.322152
Down	CDKN3	32	0.003019	1564204	0.302991
Down	COL4A1	31	0.001704	998644	0.318825
Down	VCAN	31	0.002243	3325576	0.281515
Down	TNFAIP6	29	0.004894	3551464	0.309031
Down	BMP4	29	0.00477	6323086	0.261868
Down	DCAF4	29	0.002018	6457740	0.29138
Down	DACT1	28	0.001674	1236348	0.321216
Down	FBN2	27	0.002317	1481936	0.317068
Down	FBN1	27	0.001379	1080758	0.307209
Down	CPA4	27	0.002556	996084	0.289201
Down	PXDN	26	0.002559	2031162	0.300221
Down	CNN1	24	0.002226	1637732	0.325932
Down	GAP43	24	0.00294	1612258	0.325343
Down	FAT3	23	0.002598	2919422	0.275457
Down	KIF26B	22	0.001863	792688	0.306372

Down	CYBRD1	22	0.001123	1561118	0.291533
Down	LRRC8E	22	0.001826	2528860	0.287639
Down	SIX2	22	0.001973	2753556	0.291415
Down	POU2F2	21	0.001426	1334750	0.295316
Down	FLI1	21	0.00112	2415044	0.285052
Down	GPR161	20	0.002009	2695240	0.292303
Down	PCDH12	19	0.001536	1167904	0.272989
Down	ADAMTS2	19	0.002709	2167276	0.259404
Down	ANKRD1	19	0.001457	2414200	0.271906
Down	TEKT2	19	0.002071	3016046	0.282477
Down	COLQ	18	0.003044	3000882	0.306046
Down	MSRB3	18	0.002113	3276728	0.289003
Down	CSF2	17	1.81E-04	232386	0.284073
Down	INHBE	17	0.001905	3619024	0.291805
Down	NTM	17	0.001536	2018548	0.280112
Down	SULF2	16	0.001763	1637484	0.282677
Down	ADAMTS12	14	3.95E-04	228572	0.287916
Down	CABLES1	14	4.83E-04	277378	0.300472
Down	KANK4	14	0.002325	3632254	0.267836
Down	EBF1	14	0.001351	2657292	0.252404
Down	TGFBI	13	4.16E-04	410792	0.302748
Down	CLIC5	13	6.32E-04	350440	0.308236
Down	KLRK1	13	0.001636	1607184	0.253865
Down	SLC16A10	13	0.002048	1684164	0.231182
Down	KLHL1	12	8.40E-04	685122	0.283569
Down	ULBP1	11	0.001627	1909902	0.252616
Down	CENPL	11	0.001015	1075848	0.281835
Down	EFNA4	10	0.001001	1689268	0.262691
Down	SGCD	10	0.001345	549950	0.269018
Down	TNFRSF11B	8	8.96E-04	1069060	0.296057

Down	ERG	8	9.91E-04	1598524	0.326955
Down	PDGFB	8	2.27E-04	209072	0.266763
Down	GPX8	8	9.35E-04	811058	0.233017
Down	ADORA2B	7	8.76E-04	1026210	0.25586
Down	POSTN	6	8.80E-04	1154784	0.237699
Down	KIF6	6	8.38E-04	1734970	0.202506
Down	HLA-DQB1	5	3.89E-04	258228	0.235782
Down	NTNG2	5	1.04E-04	119956	0.2581
Down	HHATL	4	3.03E-04	173754	0.247812
Down	SRPX2	4	1.18E-05	10068	0.23472
Down	TIMP3	4	2.01E-04	158044	0.310097
Down	HCST	4	2.61E-04	63872	0.273894
Down	TCF7L1	4	1.72E-05	21986	0.253936
Down	ZBTB47	4	2.82E-04	354140	0.266063
Down	SALL4	4	1.14E-05	20262	0.267368
Down	CST6	3	5.80E-05	89820	0.250776
Down	LAMA1	3	6.11E-05	12132	0.257601
Down	NID1	3	4.30E-06	4204	0.258499
Down	BGN	3	8.53E-05	103066	0.254728
Down	PDGFRA	3	7.58E-05	77934	0.284916
Down	COL3A1	3	1.64E-06	1006	0.253096
Down	ADA	3	3.21E-05	15284	0.235058
Down	NELL2	2	2.10E-05	14054	0.246513
Down	KDR	2	2.89E-05	27088	0.254746
Down	ECEL1	2	4.32E-05	24446	0.234537
Down	STAMBPL1	2	4.96E-05	27352	0.254268
Down	SERPINE1	2	2.85E-06	2312	0.251741
Down	CD93	2	0	0	0.253811
Down	ZNF16	2	0	0	0.253811
Down	NID2	2	1.07E-06	1590	0.25443

Down	IGDCC4	2	1.01E-04	72314	0.262566
Down	ECM1	2	4.51E-06	13198	0.248764
Down	F2R	2	2.19E-05	6442	0.256902
Down	ASPM	2	1.17E-04	27730	0.255107
Down	THBS2	2	0	0	0.264556
Down	COL5A3	2	0	0	0.251187
Down	GREM2	2	1.13E-06	1018	0.207542
Down	COL14A1	2	3.69E-05	13532	0.278335
Down	GLRA1	2	0	0	0
Down	LDHAL6A	2	8.46E-06	18176	0.280834
Down	MFAP2	2	0	0	0.242474
Down	MST1R	2	2.48E-05	76094	0.293269
Down	FOXQ1	2	2.41E-06	5328	0.256728
Down	PRR11	2	3.99E-06	4210	0.259441
Down	PLAU	2	3.89E-06	3598	0.246159
Down	RGS5	2	3.15E-05	39976	0.279535
Down	HCLS1	2	1.38E-05	64778	0.279764
Down	RASSF9	2	0	0	0.279275
Down	CAPN3	2	1.29E-04	71456	0.26935
Down	EMCN	2	3.95E-06	4814	0.206713
Down	PTPRE	1	0	0	0.244935
Down	GHR	1	0	0	0.24974
Down	KIF14	1	0	0	0.23932
Down	FRMD5	1	0	0	0.23932
Down	TBC1D2	1	0	0	0.246809
Down	MMP11	1	0	0	0.246758
Down	ENPEP	1	0	0	0.234483
Down	NGF	1	0	0	0.249376
Down	DDR2	1	0	0	0.251609
Down	AMPD3	1	0	0	0.259778

Down	KRT6B	1	0	0	0.259778
Down	PALMD	1	0	0	0.304543
Down	BACH2	1	0	0	0.304543
Down	NOX5	1	0	0	0.304543
Down	USP6	1	0	0	0.304543
Down	MCAM	1	0	0	0.263412
Down	LUM	1	0	0	0.247744
Down	CTSK	1	0	0	0.241847
Down	CMTM3	1	0	0	0.245219
Down	FAT4	1	0	0	0.248884
Down	COL12A1	1	0	0	0.256554
Down	ACSM3	1	0	0	0.274867
Down	LAMA4	1	0	0	0.24227
Down	PHLDA1	1	0	0	0.253159
Down	ZNF74	1	0	0	0.263094
Down	NLRP1	1	0	0	0.236161
Down	IL18	1	0	0	0.236161
Down	MFAP4	1	0	0	0.235019
Down	APOBEC3B	1	0	0	0.27675
Down	SPOCD1	1	0	0	0.27675
Down	GPRC5A	1	0	0	0.258853
Down	E2F7	1	0	0	0.244776
Down	NRG3	1	0	0	0.205779
Down	S1PR3	1	0	0	0.257113
Down	TAF4B	1	0	0	0.28167
Down	NRBP2	1	0	0	0.238756
Down	SYNPO2	1	0	0	0.267328
Down	MMS22L	1	0	0	0.256006
Down	TIPIN	1	0	0	0.256006
Down	ACOX2	1	0	0	0.231323

Down	CCNJL	1	0	0	0.240079
Down	ZNF564	1	0	0	0.242793
Down	COLEC11	1	0	0	0.24466
Down	RTEL1	1	0	0	0.237785
Down	CHL1	1	0	0	0.304543
Down	BCAS1	1	0	0	0.304543
Down	DCX	1	0	0	0.245219
Down	COL6A3	1	0	0	0.241643
Down	EGF	1	0	0	0.253159
Down	ZSCAN20	1	0	0	0.242605
Down	IFITM1	1	0	0	0.256106
Down	STK10	1	0	0	0.256106
Down	HRH1	1	0	0	0.256106
Down	PECAM1	1	0	0	0.252041
Down	PCK1	1	0	0	0.257113
Down	S1PR1	1	0	0	0.257113
Down	MYL9	1	0	0	0.252714
Down	SLC7A5	1	0	0	0.252714
Down	GATA4	1	0	0	0.238613
Down	RASSF2	1	0	0	0.236417
Down	CDCA7L	1	0	0	0.24466
Down	ISLR	1	0	0	0.24466
Down	GPC3	1	0	0	0.201677
Down	EFNB2	1	0	0	0.233486
Down	HEY2	1	0	0	0.245018

Table 6 miRNA - hub gene and TF – hub gene interaction

Regulation	Hub Genes	Degree	MicroRNA	Regulation	Hub Genes	Degree	TF
Up	MRPL12	102	hsa-mir-1255b-5p	Up	JUN	62	VDR
Up	RAB5C	100	hsa-mir-499a-5p	Up	POLR2A	45	BACH1

Up	VCAM1	86	hsa-mir-200a-3p	Up	HIF1A	39	TFCP2L1
Up	HIF1A	84	hsa-mir-449c-5p	Up	MRPL12	36	HOXC9
Up	CLU	69	hsa-mir-520a-5p	Up	U2AF2	34	GATA2
Up	U2AF2	56	hsa-mir-3144-5p	Up	RELA	34	FOXO3
Up	OCRL	55	hsa-mir-95-5p	Up	PPP1CC	32	SOX2
Up	PPP1CC	49	hsa-mir-4643	Up	ADRB2	27	GATA1
Up	RELA	41	hsa-mir-1303	Up	ERBB3	25	STAT1
Up	ERBB3	40	hsa-mir-4732-5p	Up	SNCA	25	RUNX2
Up	JUN	38	hsa-mir-3178	Up	CD81	22	XRN2
Up	CD81	23	hsa-mir-552-3p	Up	SDHA	22	ESR1
Up	POLR2A	16	hsa-mir-744-5p	Up	VCAM1	16	EP300
Up	SDHA	5	hsa-mir-760	Up	ALB	12	STAT3
Up	SNCA	4	hsa-mir-7-5p	Up	OCRL	9	TEAD4
Down	CDK1	52	hsa-mir-410-3p	Down	RPTOR	52	TBX3
Down	CHEK1	52	hsa-mir-3941	Down	FN1	46	ATF3
Down	TK1	45	hsa-mir-181d-3p	Down	ANLN	42	GATA4
Down	KIT	25	hsa-mir-181c-5p	Down	MME	31	PAX6
Down	TOP2A	17	hsa-mir-708-5p	Down	HEY1	28	FOXP1
Down	FN1	8	hsa-mir-140-3p	Down	TK1	28	SOX11
Down	MCM6	6	hsa-mir-34a-5p	Down	PTN	27	SOX17
Down	ANLN	5	hsa-mir-497-5p	Down	CHEK1	27	HOXB4
Down	HEY1	4	hsa-mir-30b-5p	Down	TOP2A	25	RUNX1
Down	RPTOR	3	hsa-mir-27a-3p	Down	MCM6	24	HNF4A
Down	A2M	3	hsa-mir-98-5p	Down	FLNC	21	RNF2
Down	MME	2	hsa-mir-1-3p	Down	CDK1	19	FOXM1
Down	FLNC	2	hsa-mir-454-3p	Down	RIPK3	16	NACC1
Down	PTN	1	hsa-mir-155-5p	Down	A2M	14	FOXA2
Down	ACTA2	1	hsa-mir-484	Down	ACTA2	14	SMAD4

Figures

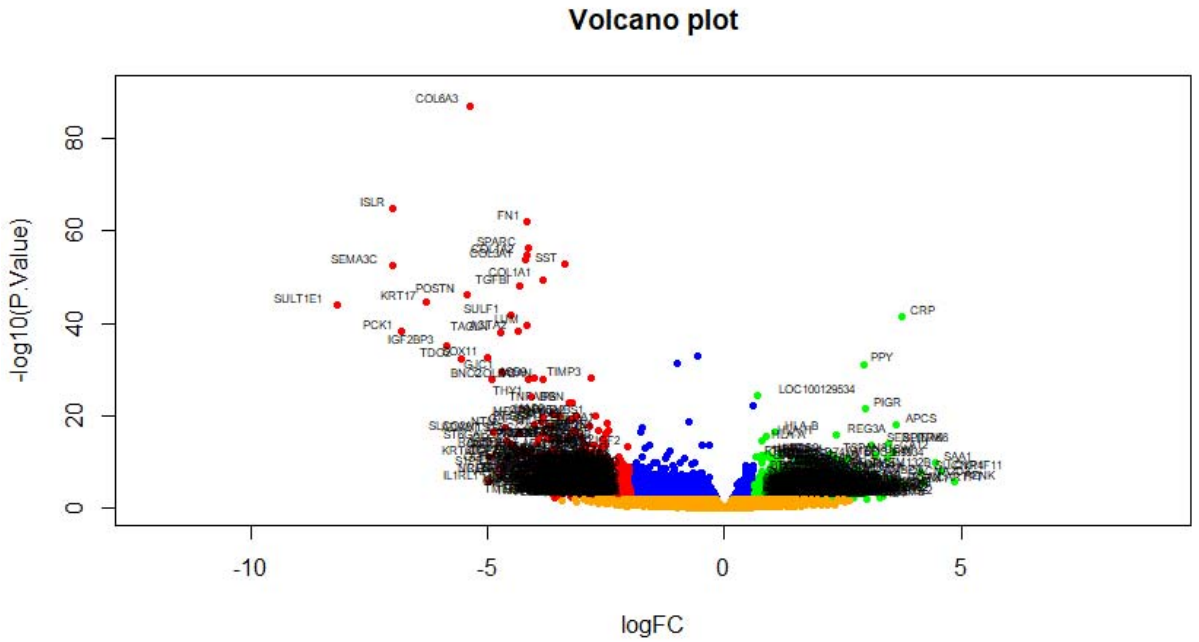

Fig. 1. Volcano plot of differentially expressed genes. Genes with a significant change of more than two-fold were selected. Green dot represented up regulated significant genes and red dot represented down regulated significant genes.

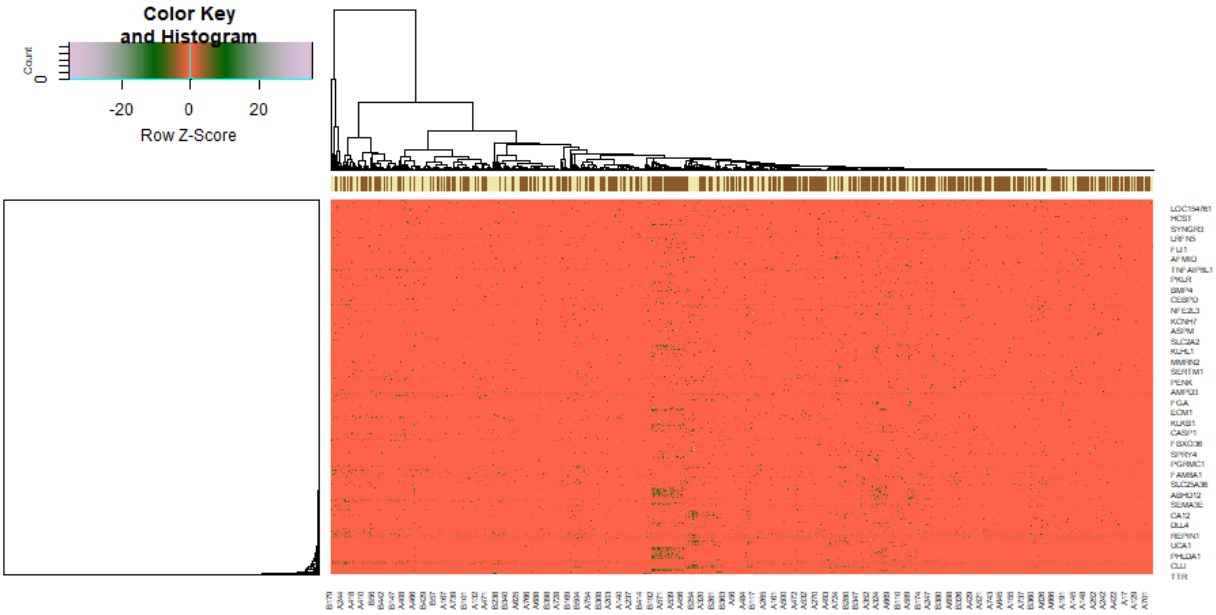

Fig. 2. Heat map of differentially expressed genes. Legend on the top left indicate log fold change of genes. (A1 – A508= normal control; B1 – B508 = T2DM)

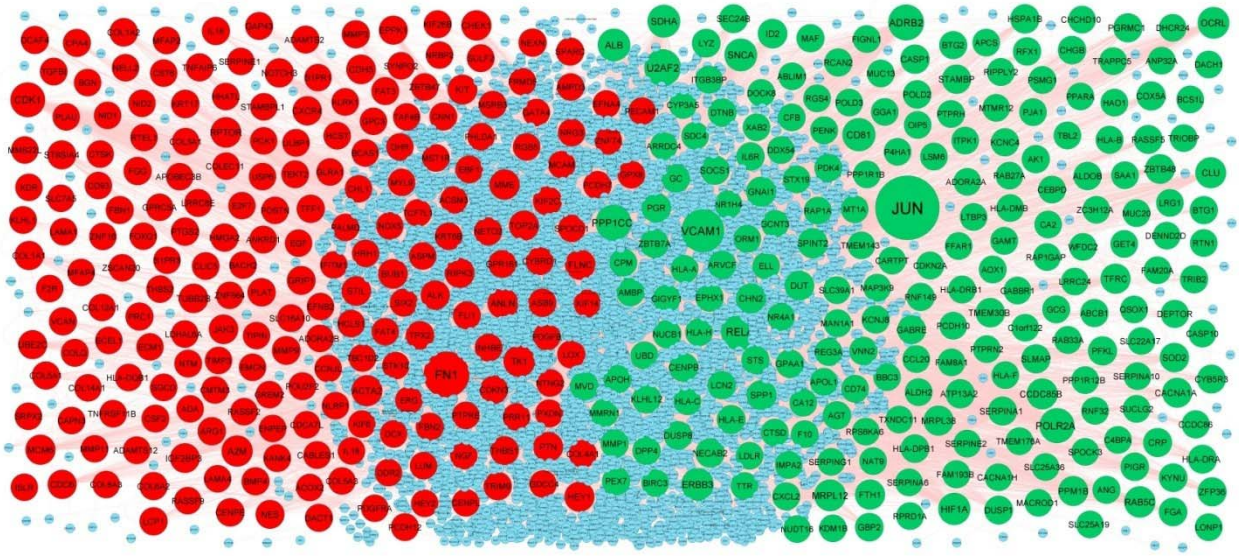

Fig. 3. PPI network of DEGs. The PPI network of DEGs was constructed using Cytoscap. Up regulated genes are marked in green; down regulated genes are marked in red

Fig. 4. Modules of isolated form PPI of DEGs. (A) The most significant module was obtained from PPI network with 48 nodes and 104 edges for up regulated genes (B) The most significant module was obtained from PPI network with 30 nodes and 92 edges for down regulated genes. Up regulated genes are marked in green; down regulated genes are marked in red.

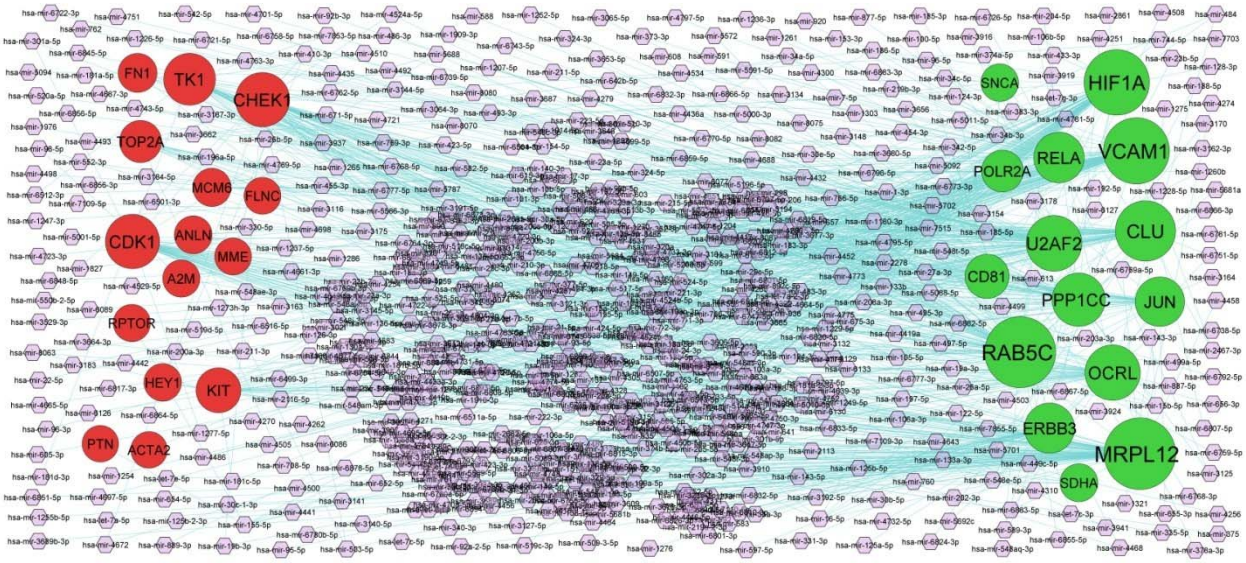

Fig. 5. MiRNA - hub gene regulatory network. The purple color diamond nodes represent the key miRNAs; up regulated genes are marked in green; down regulated genes are marked in red.

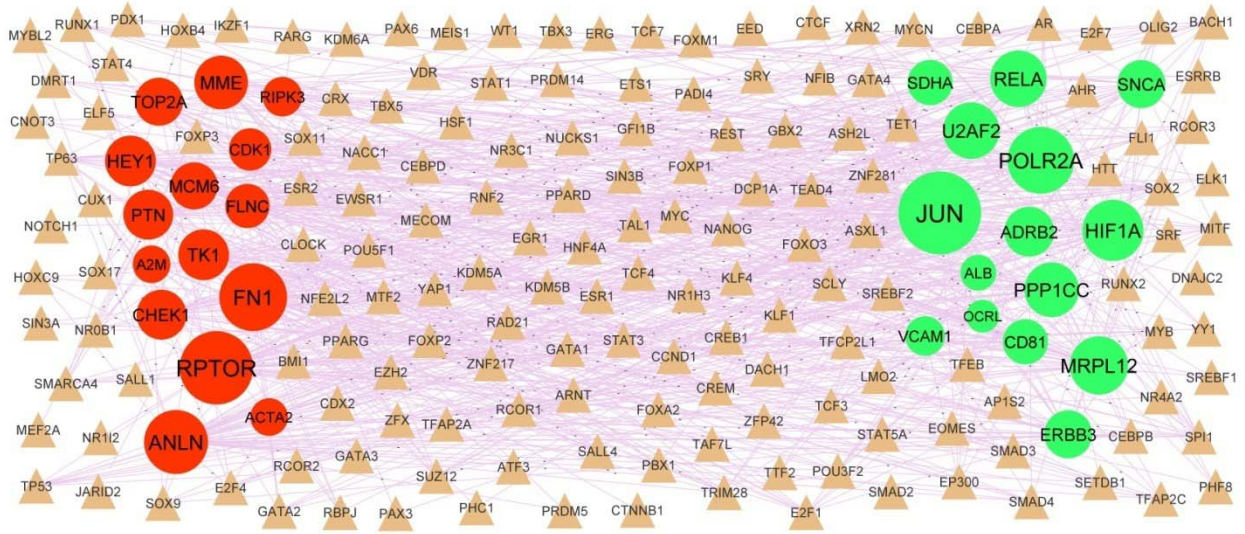

Fig. 6. TF - hub gene regulatory network. The brown color triangle nodes represent the key TFs; up regulated genes are marked in green; down regulated genes are marked in red.

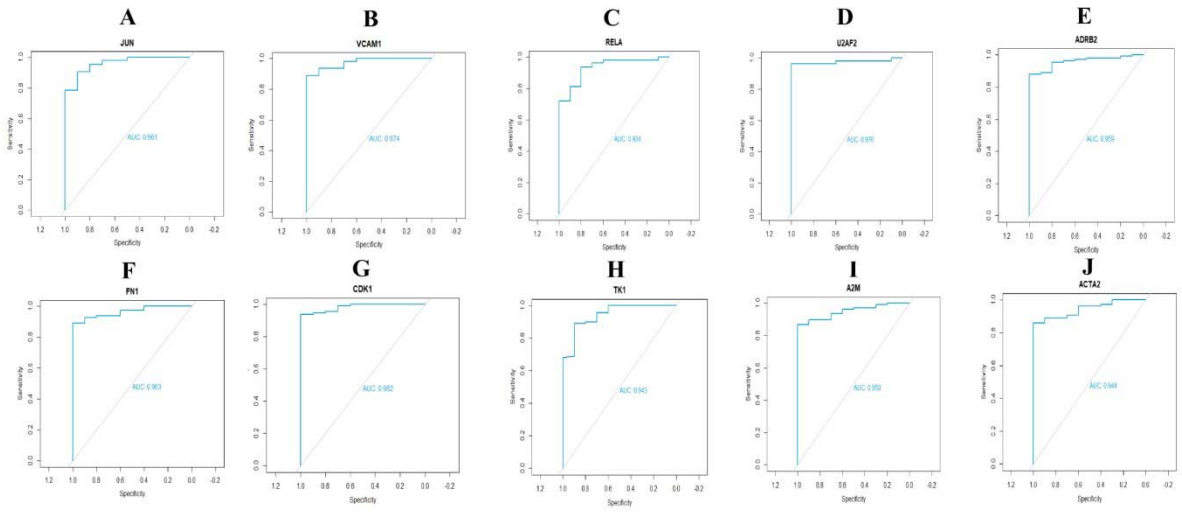

Fig. 7 ROC curve validated the sensitivity, specificity of hub genes as a predictive biomarker for T2DM prognosis. A) JUN B) VCAM1C) RELA D) U2AF2 E) ADRB2 F) FN1 G) CDK1 H) TK1 I) A2M J) ACTA2

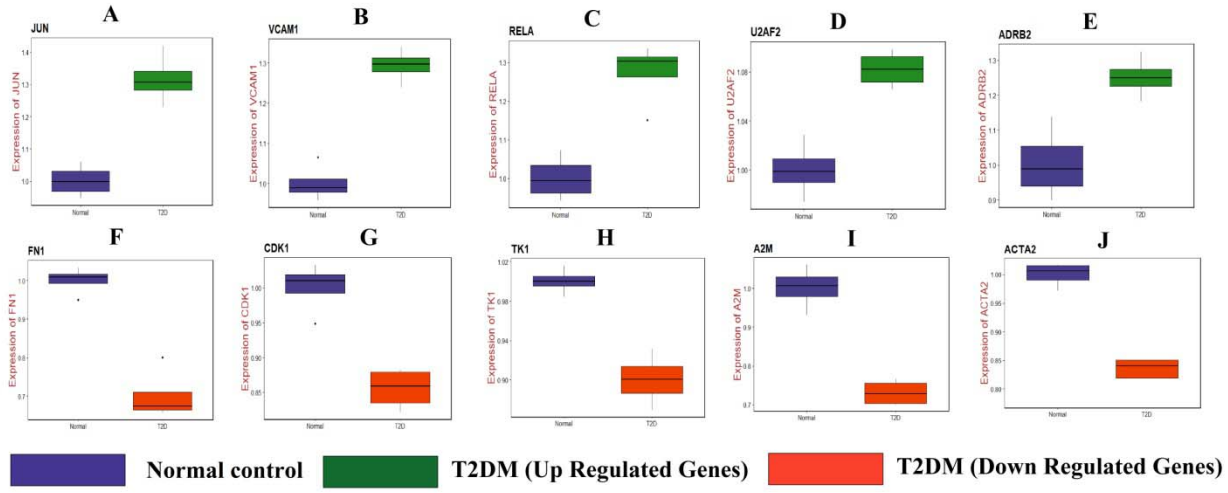

Fig. 8 Validation of hub genes by RT- PCR. A) JUN B) VCAM1C) RELA D) U2AF2 E) ADRB2 F) FN1 G) CDK1 H) TK1 I) A2M J) ACTA2