Identification of candidate biomarkers and pathways associated with type 1 diabetes mellitus using bioinformatics analysis

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Abstract

Type 1 diabetes mellitus (T1DM) is a metabolic disorder for which the underlying molecular mechanisms remain largely unclear. This investigation aimed to elucidate essential candidate genes and pathways in T1DM by integrated bioinformatics analysis. In this study, differentially expressed genes (DEGs) were analyzed using DESeq2 of R package from GSE162689 of the Gene Expression Omnibus (GEO). Gene ontology (GO) enrichment analysis, REACTOME pathway enrichment analysis, and construction and analysis of protein-protein interaction (PPI) network, modules, miRNA-hub gene regulatory network and TF-hub gene regulatory network, and validation of hub genes were then performed. A total of 952 DEGs (477 up regulated and 475 down regulated genes) were identified in T1DM. GO and REACTOME enrichment result results showed that DEGs mainly enriched in multicellular organism development, detection of stimulus, diseases of signal transduction by growth factor receptors and second messengers, and olfactory signaling pathway. The top hub genes such as MYC, EGFR, LNX1, YBX1, HSP90AA1, ESR1, FN1, TK1, ANLN and SMAD9 were screened out as the critical genes among the DEGs from the PPI network, modules, miRNA-hub gene regulatory network and TF-hub gene regulatory network. Receiver operating characteristic curve (ROC) analysis and RT-PCR confirmed that these genes were significantly associated with T1DM. In conclusion, the identified DEGs, particularly the hub genes, strengthen the understanding of the advancement and progression of T1DM, and certain genes might be used as candidate target molecules to diagnose, monitor and treat T1DM.

Keywords: differentially expressed genes; Type 1 diabetes mellitus; bioinformatics analysis; biomarkers; protein-protein interaction network

Introduction

Type 1 diabetes mellitus (T1DM) is chronic autoimmune diabetes characterized by autoimmune mediated destruction of pancreatic beta cells [1]. T1DM is most generally identified in children and adolescents [2]. Epidemiological studies have shown that the incidence of T1DM has been increasing by 2% to 5% globally [3]. T1DM is a complex disease affected by numerous environmental factors, genetic factors and their interactions [4-5]. Several complication of T1DM such as cardiovascular disease [6], hypertension [7], diabetic retinopathy [8], diabetic nephropathy [9], diabetic neuropathy [10], obesity [11] and cognitive impairment [12]. Therefore, exploring the molecular mechanism of T1DM development and its associated biomarkers to improve the early diagnosis and treatment of T1DM.

Although the remarkable improvement is achieved in the treatment of T1DM is insulin therapy [13], the long-term survival rates of T1DM still remain low worldwide. One of the major reasons is that most patients with T1DM were diagnosed at advanced stages. It is crucial to find out new therapeutic targets and novel diagnostic biomarkers for the early diagnosis and timely treatment of T1DM. Therefore, it is still urgent to further explore the exact molecular mechanisms of the development of T1DM. At present, several genes and signaling pathway are identified; for example vitamin D receptor (VDR) [14], HLA-B and HLA-A [15], HLA-DQ [16], HLA□DQB1, HLA□DQA1 and HLA□DRB1 [17], IDDM2 [18], CaMKII/NF-κB/TGF-β1 and PPAR-γ signaling pathway [19], Keap1/Nrf2 signaling pathway [20], HIF-1/VEGF pathway [21], NLRP3 and NLRP1 inflammasomes signaling pathway [22] and NO/cGMP signaling pathway [23]. Therefore, it is of great practical significance to explore the genes and signaling pathways of T1DM on β islet cells.

High-throughput RNA sequencing platform for gene expression analysis have been increasingly recognized as approaches with significant clinical value in areas such as molecular diagnosis, prognostic prediction and identification of novel therapeutic targets [24]. RNA sequencing analysis has been widely used in various gene expression profiling studies examining disease pathogenesis in the last decade, and has revealed many differentially expressed genes (DEGs) associated in various pathways, biological processes, and molecular functions. We therefore used an expression profiling by high throughput sequencing dataset to investigate the pathogenesis of T1DM.

We downloaded expression profiling by high throughput sequencing dataset GSE162689 [25], from Gene Expression Omnibus database (GEO) (http://www.ncbi.nlm.nih.gov/geo/) [26], which contain gene expression data from T1DM samples and normal control samples. We then performed deep bioinformatics analysis, including identifying common differential expressed genes (DEGs), gene ontology (GO) enrichment analysis, REACTOME pathway enrichment analysis, and construction and analysis of protein-protein interaction (PPI) network, modules, miRNA-hub gene regulatory network and TF-hub gene regulatory network. The findings were further validated by receiver operating characteristic curve (ROC) analysis and RT-PCR. The aim of this study was to identify DEGs and important pathways, and to explore potential candidate biomarkers for the diagnosis, prognosis and therapeutic targets in T1DM.

Materials and methods

Data resources

Expression profiling by high throughput sequencing dataset GSE162689 [25] was obtained from GEO database. The dataset comprised total 59 samples, of which 27 were from T1DM samples and 32 were from normal control samples and was based on the GPL24014 Ion Torrent S5 XL (Homo sapiens).

Identification of DEGs

Differentially expressed genes (DEGs) between T1DM and normal control samples were identified by using the DESeq2 package on R language software [27]. DEGs were considered when an adjusted $P < 0.05$, and a $|\log 2 \text{ fold change}| > 0.63$ for up regulated genes and $|\log 2 \text{ fold change}| < -1.3$ for down regulated genes. The adjusted P values, by employing Benjamini and Hochberg false discovery rate [28], were aimed to correct the occurrence of false positive results. The DEGs were presented in volcano plot and heat map drawn using a plotting tool ggplot2 and gplots based on the R language.

GO and REACTOME pathway enrichment analysis of DEGs

One online tool, g:Profiler (http://biit.cs.ut.ee/gprofiler/) [29], was applied to carried out the functional annotation for DEGs. Gene Ontology (GO) (http://geneontology.org/) [30] generally perform enrichment analysis of genomes. And there are mainly biological processes (BP), cellular components (CC) and molecular functions (MF) in the GO enrichment analysis. REACTOME (https://reactome.org/) [31] is a comprehensive database of genomic, chemical, and systemic functional information. Therefore, g:Profiler was used to make enrichment analysis of GO and REACTOME. $P < 0.05$ was set as the cutoff criterion.

Construction of the PPI network and module analysis

PPI network was established using the IntAct Molecular Interaction Database (https://www.ebi.ac.uk/intact/) [32]. To assess possible PPI correlations, previously identified DEGs were mapped to the IntAct database, followed by extraction of PPI pairs with a combined score >0.4. Cytoscape 3.8.2 software (www.cytoscape.org/) [33] was then employed to visualize the PPI network, and the Cytoscape plugin Network Analyzer was used to calculate the node degree [34], betweenness centrality [35], stress centrality [36] and closeness centrality [37] of each protein node. Specifically, nodes with a higher node degree, betweenness centrality, stress centrality and closeness centrality were likely to play a more vital role in maintaining the stability of the entire network. The PEWCC1 (http://apps.cytoscape.org/apps/PEWCC1) [38] plug-in was applied to analyze the modules in the PPI networks, with the default parameters (node score = 0.2, K-core$\geqq$2, and max depth = 100).

MiRNA-hub gene regulatory network construction

The miRNAs targeting the T1DM related were predicted using the miRNet database (https://www.mirnet.ca/) [39], and those predicted by at least 14 databases (TarBase, miRTarBase, miRecords, miRanda, miR2Disease, HMDD, PhenomiR, SM2miR, PharmacomiR, EpimiR, starBase, TransmiR, ADmiRE, and TAM 2.0) were selected for constructing the miRNA-hub gene regulatory network by Cytoscape 3.8.2 software.

TF-hub gene regulatory network construction

The TFs targeting the T1DM related were predicted using the NetworkAnalyst database (https://www.networkanalyst.ca/) [40], and those predicted by RegNetwork database was selected for constructing the TF-hub gene regulatory network by Cytoscape 3.8.2 software.

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

A ROC curve analysis is an approach for visualizing, organizing and selecting classifiers based on their achievement of hub genes. A diagnostic test was firstly performed in order to estimate the diagnostic value of hub genes in T1DM. ROC curves were obtained by plotting the sensitivity, against the specificity using the R package “pROC” [41]. Area under the curve (AUC) was used to measure the accuracy of these diagnostic values of the hub genes. An AUC□>□0.9 determined that the model had a favorable fitting effect.

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

Pancreatic beta MIN6 cells were maintained in Dulbecco’s minimal essential medium (DMEM) supplemented with 15 % fetal calf serum, 50 mg/l streptomycin and 75 mg/l penicillin sulphate. MIN6 cells treated with streptozotocin for T2DM and MIN6 cells untreated for normal control. All treated MIN6 cells and untreated MIN6 cells were incubated at 37 ◦C, 5% CO_2 in humidified incubator. Total RNA was extracted from the treated and untreated cells using TRI reagent (Sigma, USA) according to the manufacturer’s protocol. Reverse transcription kit (Thermo Fisher Scientific, Waltham, MA, USA) was used for Converting mRNA to cDNA. Expression levels of mRNAs were determined by RT-PCR using QuantStudio 7 Flex real-time PCR system (Thermo Fisher Scientific, Waltham, MA, USA). The protocol was set as follows: 50□°C for 2□min, 95□°C for 10□min, 40□cycles of 95□°C for 10□s, 60□°C for 30□s. All the samples were normalized to the corresponding expression of internal control β-actin . The test was performed in triplicate and the relative expression levels were calculated with the $2^{-\Delta\Delta Ct}$ method [42]. Table 1 is given for primer sequences used in the RT-PCR.

Results

Identification of DEGs

On the basis of the cut□off criteria, DEGs in GEO dataset was identified between T1DN and normal control samples (Table 2). There were 952 DEGs, including 477 up regulated and 475 down regulated genes in GSE162689 with the threshold of adjusted $P < 0.05$, and a |log2 fold change| > 0.63 for up regulated genes and |log2 fold change| < -1.3 for down regulated genes. The volcano plot of the distribution of DEGs in is shown in Fig. 1. The expression heat map of the DEGs is shown in Fig. 2.

GO and REACTOME pathway enrichment analysis of DEGs

To characterize the functional roles of the above DEGs, we used GO (Table 3) and REACTOME pathway (Table 4) enrichment analyses. The BP category of the GO analysis results showed that up regulated genes were significantly enriched in multicellular organism development and nitrogen compound metabolic process. For CC, these up regulated were enriched in membrane-enclosed lumen and nuclear lumen. Moreover, up regulated genes were significantly enriched in protein binding and transcription regulator activity in the MF categories. In addition, the most significantly enriched GO terms for down regulated genes were detection of stimulus and multicellular organismal process (BP), cell periphery and plasma membrane (CC), and transmembrane signaling receptor activity and molecular transducer activity (MF). According to REACTOME pathway enrichment analysis, up regulated genes were significantly enriched in diseases of signal transduction by growth factor receptors and second messengers and formation of the cornified envelope. Down regulated genes were enriched in olfactory signaling pathway and sensory perception.

Construction of the PPI network and module analysis

The PPI network of the DEGs was constructed with 5111 nodes and 9392 edges by using the IntAct database (Fig. 3). A node with a higher node degree, betweenness centrality, stress centrality and closeness centrality consider as a hub genes and are listed in Table 5. The key points of the network include the up regulated hub genes, such as MYC, EGFR, LNX1, YBX1 and HSP90AA1, and the down regulated hub genes, such as ESR1, FN1, TK1, ANLN and SMAD9. To detect significant modules in the PPI network, the PEWCC1 plug□in was used for analysis, and two modules that had the highest degree stood out. GO and pathway enrichment analysis showed that module 1 contained 28 nodes and 63 edges (Fig.4A), which were associated with diseases of signal transduction by growth factor receptors and second messengers, disease, nitrogen compound metabolic process and membrane-enclosed lumen, while module 2 had 14 nodes and 30 edges (Fig.4B), which were mainly associated with signal transduction, multicellular organismal process and detection of stimulus.

MiRNA-hub gene regulatory network construction

The network of miRNAs and predicted targets (hub genes) is presented in Table 6. Based on the miRNAs, a miRNA -hub gene regulatory network was constructed with 2568 nodes (miRNA: 2259; hub gene: 309) and 16618 interaction pairs (Fig.5). Notably, MYC targeted 194 miRNAs, including hsa-mir-4677-3p; HSP90AA1 targeted 188 miRNAs, including hsa-mir-3125; FKBP5 targeted 116 miRNAs, including hsa-mir-4779; RNPS1 targeted 109 miRNAs, including hsa-mir-548az-3p; SQSTM1 targeted 108 miRNAs, including hsa-mir-106a-5p; ANLN targeted 127 miRNAs, including hsa-mir-664a-3p; CDK1 targeted 109 miRNAs, including hsa-mir-5688;FN1 targeted 105 miRNAs, including hsa-mir-199b-3p;ESR1 targeted 98 miRNAs, including hsa-mir-206; TK1 targeted 80 miRNAs, including hsa-mir-6512-3p.

TF-hub gene regulatory network construction

The network of TFs and predicted targets (hub genes) is presented in Table 6. Based on the TFs, a TF -hub gene regulatory network was constructed with 899 nodes (TF: 604; hub gene: 295) and 3542 interaction pairs (Fig.6). Notably, MAPK3 targeted 48 TFs, including JUND; HSP90AA1 targeted 35 TFs, including HSF2; SQSTM1 targeted 34 TFs, including SMAD4; STUB1 targeted 31 TFs, including ATF6; EGFR targeted 27 TFs, including ELF3; ESR1 targeted 126 TFs, including ELF3; SMAD9 targeted 38 TFs, including ELF3; CDK1 targeted 36 TFs, including ELF3; FN1 targeted 25 TFs, including ELF3; NEK6 targeted 16 TFs, including ELF3.

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

ROC curve analysis was for evaluating the capacity of MYC, EGFR, LNX1, YBX1, HSP90AA1, ESR1, FN1, TK1, ANLN and SMAD9, so as to distinguish T1DM from normal control (Fig.7). ROC curve analysis showed that MYC, EGFR, LNX1, YBX1, HSP90AA1, ESR1, FN1, TK1, ANLN and SMAD9 expression levels have potential diagnostic value for T1DM patients (AUC□>□0.9).

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

Next, in order to verify the results of previous bioinformatics analysis, the gene expression levels of MYC, EGFR, LNX1, YBX1, HSP90AA1, ESR1, FN1, TK1, ANLN and SMAD9 were detected by RT-PCR between T1DM and normal control. As shown in Fig 8, compared with normal tissues, MYC, EGFR, LNX1, YBX1 and HSP90AA1 mRNA expression levels were significantly up regulated in the T1DM, and ESR1, FN1, TK1, ANLN and SMAD9 mRNA level were down regulated, which was consistent with the results of bioinformatics analysis.

Discussion

T1DM is the common forms of chronic autoimmune diabetes that affect an individual's quality of life [43]. However, the potential causes of T1DM remain uncertain. Understanding the underlying molecular pathogenesis of T1DM is of key importance for diagnosis, prognosis, and identifying drug targets. As high-throughput RNA sequencing can provide information regarding the expression levels of thousands of genes in the human genome simultaneously, this methodology has been widely used to predict the potential diagnostic and therapeutic targets for T1DM. In the present investigation, we extracted the data from GSE162689, which includes 27 T1DM samples and 32 normal control samples. We identified 477 up regulated and 475 down regulated genes between T1DM samples and normal control samples using bioinformatics analysis. FGA (fibrinogen alpha chain) [44] and FGB (fibrinogen beta chain) [45] genes have been found to be expressed in cardiovascular disease, but these genes might be novel target for T1DM. IGF2 [46], IAPP (islet amyloid polypeptide) [47], INS (insulin) [48] and MAFA (MAF bZIP transcription factor A) [49] have been reported be associated with the development of T1DM. Previous study have indicated the expression of ADCYAP1 is associated in type 2 diabetes mellitus [50], but this gene might be novel target for T1DM. Gold et al. [51] found the

CSNK1G1 was a prognostic factor in cognitive impairment, but this gene might be novel target for T1DM.

Furthermore, we investigated the biological functions of these DEGs by using online website, and GO and pathway enrichment analysis. Husemoen et al [52], Zhang et al [53], Hartz et al [54], Słomiński et al [55], Johansson et al [56], Pan et al [57], Lopez-Sanz et al [58], Grant, [59], Słomiński et al [60], Galán et al [61], Jordan et al [62], Winkler et al [63], Yip et al [64], Crookshank et al [65], Lempainen et al [66], Qu and Polychronakos, [67], Morrison et al [68], Zhang et al [69], Gerlinger-Romero et al [70], Belanger et al [71], Dieter et al [72], Wanic et al [73], Ushijima Wanic et al [74], Guo et al [75], Davis et al [76], Elbarbary et al [77], Villasenor et al [78], Zhang et al [79], Lee et al [80], Zhi et al [81], Li Calzi et al [82], Sebastiani et al [83], Cherney et al [84], Doggrell, [85] and Yanagihara et al [86] found that FLG (filaggrin), FGF21, PEMT (phosphatidylethanolamine N-methyltransferase) KL (klotho), CEL (carboxyl ester lipase), FOSL2, STAT1, TCF7L2, TP53, EGFR (epidermal growth factor receptor), ETS1, KCNJ8, DEAF1, GCG (glucagon), IKZF4, OAS1, IRS1, ABCG2, FBXO32, PTBP1, BACH2, CNDP2, KLF11, MT1E, DPP4, SLC29A3, RGS16, MAS1, GCGR (glucagon receptor), HLA-C, VASP (vasodilator stimulated phosphoprotein), CCR2, PTGS2, GLP1R and JMJD6 are involved in the progression of T1DM. Vassilev et al [87], Qin et al [88], Ma et al [89], West et al [90], Hoffmann et al [91], Deary et al [92], Belangero et al [93], Jung et al [94], Tang et al [95], Goodier et al [96], Petyuk et al [97], Roux et al [98], Castrogiovanni et al [99], Suleiman et al [100], Haack et al [101], Kwiatkowski et al [102], Pinacho et al [103], Luo et al [104], He et al [105], Moudi et al [106], Thevenon et al [107], Li et al [108], Reitz et al [109], Jenkins and Escayg [110], Letronne et al [111], Ma et al [112], Chabbert et al [113], Abramsson et al [114], Aeby et al [115] and Roll et al [116] found that the expression of DCC (DCC netrin 1 receptor), PLP1, SNX19, SH3RF1, TNFRSF1A, NCSTN (nicastrin), DGCR2, NPAS2, CDNF (cerebral dopamine neurotrophic factor), SMCR8, HSPA2, STUB1, CHID1, ATP13A2, SQSTM1, LIG3, SP4, ACSL6, ERN1, ATF6B, LRFN2, NRG3, LRRTM3, GABRA2, ADAM30, GABRR2, TSHZ3, LOXL1, SCN1B and SRPX2 are associated with the prognosis of patients with cognitive impairment, but these genes might be novel target for T1DM. Recent studies found that KCP (kielin cysteine rich BMP regulator) [117], NOG (noggin) [118], COL6A3 [119], BTG2 [120], RPS6 [121], KLF15 [122], KLF3 [123], ZFP36 [124], ETV5 [125], TLE3 [126], NNMT (nicotinamide N-methyltransferase) [127], WDTC1 [128], ZFHX3 [129], SIAH2 [130], MBOAT7 [131], RUNX1T1 [132], MAPK4 [133], KLF9 [134], SELENBP1 [135], HELZ2 [136], ELK1 [137], SERTAD2 [138], CRTC3 [139], ABCB11 [140], TACR1 [141], SLC22A11 [142], PER3 [143], P2RX5 [144], MFAP5 [145], FGL1 [146], OLFM4 [147], NTN1 [148], ESR1 [149], ABCB1 [150], VAV3 [151] and LAMB3 [152] plays an important role in the occurrence and development of obesity, but these genes might be novel target for T1DM. STAR (steroidogenic acute regulatory protein) [153], IL1RN [154], AQP5 [155], EGR1 [156], SFTPD (surfactant protein D) [157], KLF10 [158], PODXL (podocalyxin like) [159], FOXN3 [160], IL6R [161], PBX1 [162], APOD (apolipoprotein D) [163], ACVR2B [164], CD34 [165], INSR (insulin receptor) [166], APOA5 [167], STAR (steroidogenic acute regulatory protein) [168], PDK4 [169], GLS (glutaminase) [170], FKBP5 [171], SLC6A15 [172], MT2A [173], SLC38A4 [174], AQP7 [175], ABHD15 [176], ABCA1 [177], ZNRF1 [178], PPP1R3B [179], MAOA (monoamine oxidase A) [180], UBE2E2 [181], RNASEK (ribonuclease K) [182], PREX1 [183], DGKG (diacylglycerol kinase gamma) [184], POSTN (periostin) [185], COMP (cartilage oligomeric matrix protein) [186], GAP43 [187], P2RY12 [188], SELL (selectin L) [189] and DLG2 [190] have been revealed to be associated with type 2 diabetes mellitus, but these genes might be novel target for T1DM. Expression of ERRFI1 [191], ALOX12 [192], SOCS5 [193], DDIT4 [194], DUSP4 [195], IL6ST [196], DUSP1 [197], SMAD1 [198], NCL (nucleolin) [199], METTL14 [200], FMOD (fibromodulin) [201], CYGB (cytoglobin) [202], UNC5A [203] and TAAR9 [204] are associated with prognosis in patients with diabetic nephropathy, but these genes might be novel target for T1DM. A previous study reported that FAP (fibroblast activation protein alpha) [205], EYA4 [206], BCL9 [207], IRF2BP2 [208], EGR3 [209], GADD45B [210], DMD (dystrophin) [211], LSR (lipolysis stimulated lipoprotein receptor) [212], DLL4 [213], SUN2 [214], SOS1 [215], PIK3CA [216], GAMT (guanidinoacetate N-methyltransferase) [217], RBM47 [218], HSP90AA1 [219], GAB1 [220], S1PR1 [221], EDNRB (endothelin receptor type B) [222], NFKBIA (NFKB inhibitor alpha) [223], GJA1 [224], GADD45G [225], PHLDA1 [226], CMPK2 [227], FIGN (fidgetin, microtubule severing factor) [228], KCNJ2 [229], ABCC9 [230], DIRAS3 [231], EPHX1 [232], RAB4A [233], UBIAD1 [234], CASQ2 [235], TTN (titin) [236], KCNH1 [237], JPH2 [238], OXGR1 [239], UCHL1 [240], SERPINA3 [241],

MMP28 [242], ADAMTS2 [243], P2RY1 [244], CSF2RA [245], MYO1F [246], SELPLG (selectin P ligand) [247] and SAMHD1 [248] are expressed in cardiovascular disease, but these genes might be novel target for T1DM. MAOB (monoamine oxidase B) [249], VEGFC (vascular endothelial growth factor C) [250], DBP (D-box binding PAR bZIP transcription factor) [251], MYADM (myeloid associated differentiation marker) [252], NES (nestin) [253], SMURF1 [254], EDNRB (endothelin receptor type B) [255], MUC6 [256], TOR2A [257], TNKS (tankyrase) [258], NEDD9 [259], ASIC1 [260], ADAMTS8 [261], DYSF (dysferlin) [262], SLC26A9 [263], SLC45A3 [264] and KCNQ2 [265] contributes to the progression of hypertension, but these genes might be novel target for T1DM. Yang et al [266], Zhang et al [267] and Wang et al [268] demonstrated that SYVN1, BTG1 and CFB (complement factor B) were associated with diabetic retinopathy, but these genes might be novel target for T1DM.

PPI network and modules were used to identify hub genes. The results of the present investigation might provide potential biomarkers for the diagnosis of T1DM. SMAD9 has been shown to be activated in hypertension [269], but this genes might be novel target for T1DM. MYC, LNX1, YBX1, FN1, TK1 and ANLN (anillin actin binding protein) might be the novel biomarkers for T1DM.

In this investigation, the miRNA-hub gene regulatory network and TF-hub gene regulatory network that regulates T1DM was constructed. Recent studies found that CDK1 [270], hsa-mir-199b-3p [271], JUND [272] and FOXF2 [273] plays an important role in the occurrence and development of obesity, but these genes might be novel target for T1DM. The hsa-mir-106a-5p [274], hsa-mir-206 [275], SMAD4 [276] and ATF6 [277] are a major regulator of type 2 diabetes mellitus, but these genes might be novel target for T1DM. Studies have shown that the hsa-mir-106a-5p [278] and HSF2 [279] are essential for regulating cardiovascular disease, but these genes might be novel target for T1DM. Mendes-Silva et al [280] indicated that hsa-mir-664a-3p facilitated cognitive impairment, but this gene might be novel target for T1DM. ELF3 participated in diabetic nephropathy [281], but this gene might be novel target for T1DM. SRY is crucial for hypertension progression [282], but this gene might be novel target for T1DM. RNPS1, MAPK3, NEK6, hsa-mir-4677-3p, hsa-mir-3125, hsa-mir-4779, hsa-mir-548az-3p, hsa-mir-5688, hsa-mir-6512-3p, XAB2, KHDRBS1 and RELA might be the novel biomarkers for T1DM.

In conclusion, the present investigation shows the global profile of DEGs and relative signaling pathways that might play in the initiation and progression of T1DM. In the pathogenesis of acne, the possible crucial genes are MYC, EGFR, LNX1, YBX1, HSP90AA1, ESR1, FN1, TK1, ANLN and SMAD9, and the possible important GO terms and pathways are multicellular organism development, detection of stimulus, diseases of signal transduction by growth factor receptors and second messengers, and olfactory signaling pathway. Therefore, it provides new research directions for the detection and treatment of T1DM. However, their involvement in the molecular mechanisms of disease needs further clinical studies.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

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

Informed consent

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

Availability of data and materials

The datasets supporting the conclusions of this article are available in the GEO (Gene Expression Omnibus) (https://www.ncbi.nlm.nih.gov/geo/) repository. [(GSE162689) (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE162689]

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author Contributions

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

C. V - Software and investigation

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Tables

Table 1 The sequences of primers for quantitative RT-PCR

Genes	Forward Primers	Reverse Primers
MYC	CTGTACCTCGTCCGATTCC	GCTCTTCTTCAGAGTCGCT
EGFR	TGGAGCTATGGTGTCACTG	TGAGATGTCACTTGCTGGG
LNX1	CTGTACTCGGAACTGGCTC	TGGCCATTAGTGTCCAGTC
YBX1	AAGAAGGTCATCGCAACGA	CAAATACGTCTTCCTTGGTGTC
HSP90AA1	CAATTCATCGGACGCTCTG	AGATTGATGTGCAGCTCCT
ESR1	CCTCTGGCTACCATTATGGG	AGTCATTGTGTCCTTGAATGC
FN1	TACCAAGGCTGGATGATGG	TGCATCTGTTTCTGGAGGT
TK1	AGATTCAGGTGATTCTCGGG	ACTTGTACTGGGCGATCTG
ANLN	TCCGACCACAAAGAGAAGAC	AGAGCCAGTTCTTGGTGAC
SMAD9	CACATTGGAAAGGGTGTGC	GACAAAGATGCTGCTGTCG

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

Gene Symbol	logFC	pValue	adj.P.Val	tvalue	Regulation	Gene Name
CRNN	5.712946	1.99E-09	6.00E-07	5.998709	Up	cornulin
PGA5	4.614794	6.37E-06	0.000351	4.513665	Up	pepsinogen A5
PGA4	4.56097	6.52E-06	0.000356	4.508769	Up	pepsinogen A4
PGA3	4.488203	2.38E-06	0.00017	4.718	Up	pepsinogen A3
CGA	4.197712	1.53E-05	0.000659	4.324569	Up	glycoprotein hormones, alpha polypeptide
FGA	4.148471	0.000107	0.002674	3.873135	Up	fibrinogen alpha chain
IGF2	3.675622	1.58E-06	0.000129	4.800531	Up	insulin like growth factor 2
KRT6A	3.542048	3.39E-06	0.000219	4.645643	Up	keratin 6A
FGB	3.450811	0.00024	0.004787	3.6727	Up	fibrinogen beta chain
LCE3D	3.269781	4.62E-09	1.14E-06	5.860339	Up	late cornified envelope 3D
PRR9	3.141513	2.53E-08	4.72E-06	5.571309	Up	proline rich 9
SLC6A15	3.082853	0.004861	0.038891	2.816137	Up	solute carrier family 6 member 15
APOA5	3.070951	6.13E-06	0.000342	4.521718	Up	apolipoprotein A5
SPRR3	2.937684	1.25E-05	0.000573	4.368603	Up	small proline rich protein 3
FLG	2.932836	0.000863	0.01179	3.331797	Up	filaggrin
SPRR2D	2.867184	0.000152	0.003454	3.787481	Up	small proline rich protein 2D
SPRR1B	2.866557	2.47E-05	0.000915	4.217563	Up	small proline rich protein 1B
SLITRK6	2.858672	3.81E-05	0.001252	4.118929	Up	SLIT and NTRK like family member 6
CT62	2.82068	0.000229	0.004614	3.684932	Up	cancer/testis associated 62
FGF21	2.789926	3.91E-06	0.000244	4.615907	Up	fibroblast growth factor 21
FGG	2.773228	0.001178	0.01471	3.244101	Up	fibrinogen gamma chain
TBX22	2.752029	5.13E-05	0.001556	4.049842	Up	T-box transcription factor 22
CALCR	2.747775	0.000411	0.006924	3.533141	Up	calcitonin receptor
PGC	2.688901	2.74E-05	0.000994	4.194452	Up	progastricsin
SPRR1A	2.664413	0.000477	0.007678	3.493077	Up	small proline rich protein 1A
ABCB11	2.650492	0.004481	0.036813	2.842169	Up	ATP binding cassette subfamily B member 11
USH2A	2.631238	0.002995	0.027872	2.968252	Up	usherin
OTX2	2.568693	6.44E-06	0.000354	4.511363	Up	orthodenticlehomeobox 2
HBM	2.562338	0.002326	0.023468	3.045118	Up	hemoglobin subunit mu
DCC	2.561422	0.000102	0.002565	3.885894	Up	DCC netrin 1 receptor
POTED	2.474492	0.002454	0.024342	3.028922	Up	POTE ankyrin domain family member D
MUC21	2.456424	0.005692	0.043083	2.765033	Up	mucin 21, cell surface associated
KCP	2.393659	0.001362	0.016053	3.202565	Up	kielin cysteine rich BMP regulator
RGPD3	2.363618	0.003817	0.032868	2.892895	Up	RANBP2 like and GRIP domain containing 3
NOG	2.354832	0.000792	0.01105	3.355497	Up	noggin
STAR	2.354313	0.000103	0.002597	3.882572	Up	steroidogenic acute regulatory protein
KRT16	2.299283	0.004488	0.036852	2.841684	Up	keratin 16
HSFX2	2.284692	0.000834	0.01146	3.341177	Up	heat shock transcription factor family, X-linked 2

IL1RN	2.270537	0.001478	0.017037	3.179045	Up	interleukin 1 receptor antagonist
ZSCAN10	2.266233	0.000319	0.005811	3.599153	Up	zinc finger and SCAN domain containing 10
MAGEA2	2.264446	0.000456	0.007479	3.505373	Up	MAGE family member A2
SHISA2	2.254679	2.83E-05	0.001022	4.186632	Up	shisa family member 2
TACR1	2.231669	0.001599	0.017899	3.156123	Up	tachykinin receptor 1
AQP5	2.195113	0.00015	0.003428	3.791855	Up	aquaporin 5
PRRG3	2.180564	0.005567	0.042512	2.77226	Up	proline rich and Gla domain 3
SYNDIG1	2.170655	0.002504	0.024649	3.022825	Up	synapse differentiation inducing 1
TFAP2C	2.160589	0.000396	0.006739	3.542676	Up	transcription factor AP-2 gamma
ERRFI1	2.155407	3.75E-08	6.56E-06	5.5022	Up	ERBB receptor feedback inhibitor 1
TMEM174	2.090104	7.82E-05	0.002098	3.949874	Up	transmembrane protein 174
CNTNAP4	2.08132	0.001501	0.017188	3.174485	Up	contactin associated protein family member 4
PLP1	2.069097	0.001613	0.017994	3.153457	Up	proteolipid protein 1
RUNX1T1	2.059542	8.51E-05	0.002242	3.929478	Up	RUNX1 partner transcriptional co-repressor 1
ALOX12	2.044757	0.007045	0.049709	2.694705	Up	arachidonate 12-lipoxygenase, 12S type
KRT13	2.038413	0.002945	0.027488	2.973453	Up	keratin 13
SLC7A14	1.98194	0.006299	0.0461	2.731787	Up	solute carrier family 7 member 14
SPRR2E	1.941341	0.006326	0.046256	2.730406	Up	small proline rich protein 2E
PDK4	1.930909	2.91E-10	1.25E-07	6.303686	Up	pyruvate dehydrogenase kinase 4
TENM1	1.914484	0.006644	0.047813	2.714165	Up	teneurintransmembrane protein 1
PRLHR	1.912351	0.006684	0.047973	2.712197	Up	prolactin releasing hormone receptor
HAO1	1.901548	0.004154	0.03502	2.866261	Up	hydroxyacid oxidase 1
SLC22A11	1.873469	0.006672	0.047915	2.7128	Up	solute carrier family 22 member 11
LOC729080	1.856377	0.007083	0.049857	2.692934	Up	glycine cleavage system protein H (aminomethyl carrier) pseudogene
PEMT	1.849123	7.27E-06	0.000386	4.485648	Up	phosphatidylethanolamine N-methyltransferase
LY6H	1.840253	0.0016	0.017903	3.155867	Up	lymphocyte antigen 6 family member H
FAM205A	1.836628	0.004029	0.034239	2.875852	Up	family with sequence similarity 205 member A
TMEM236	1.814489	0.000914	0.012245	3.315815	Up	transmembrane protein 236
KCNJ13	1.809864	0.004278	0.035664	2.856913	Up	potassium inwardly rectifying channel subfamily J member 13
FAP	1.803439	0.000962	0.01274	3.301429	Up	fibroblast activation protein alpha
EYA4	1.800375	0.003266	0.029605	2.941492	Up	EYA transcriptional coactivator and phosphatase 4
BTBD11	1.791996	0.002099	0.021686	3.075855	Up	BTB domain containing 11
OR5J2	1.786096	0.000858	0.011727	3.333497	Up	olfactory receptor family 5 subfamily J member 2
FBP2	1.783474	0.001941	0.020527	3.099056	Up	fructose-bisphosphatase 2
LCE3E	1.78332	0.000904	0.012149	3.318662	Up	late cornified envelope 3E
ZNF554	1.777372	0.000256	0.005002	3.656153	Up	zinc finger protein 554
OR10H1	1.769139	0.001545	0.017516	3.166037	Up	olfactory receptor family 10 subfamily H member 1
AQP7P1	1.76578	0.000244	0.004837	3.668581	Up	aquaporin 7 pseudogene 1
EGR1	1.751068	8.94E-07	7.97E-05	4.913629	Up	early growth response 1
CSGALNACT1	1.736673	0.000245	0.004842	3.666956	Up	chondroitin sulfate N-acetylgalactosaminyltransferase 1
MT2A	1.736195	7.33E-07	6.80E-05	4.952342	Up	metallothionein 2A
MAL	1.723595	5.94E-06	0.000338	4.528542	Up	mal, T cell differentiation protein
SLC38A4	1.716457	0.00026	0.00507	3.652138	Up	solute carrier family 38 member 4

GCG	1.704823	0.004274	0.035664	2.857184	Up	glucagon
OR13D1	1.699677	0.004653	0.037774	2.830118	Up	olfactory receptor family 13 subfamily D member 1
ASIC1	1.678655	0.00502	0.039748	2.805723	Up	acid sensing ion channel subunit 1
MMP16	1.671308	0.005478	0.041991	2.777507	Up	matrix metallopeptidase 16
ADAMTS8	1.657804	0.005782	0.043574	2.759899	Up	ADAM metallopeptidase with thrombospondin type 1 motif 8
PTGER4	1.653859	3.38E-07	3.75E-05	5.101075	Up	prostaglandin E receptor 4
TMEM201	1.653235	5.59E-10	2.16E-07	6.201596	Up	transmembrane protein 201
FLJ40194	1.624297	0.004189	0.035182	2.863583	Up	uncharacterized FLJ40194
SPATA31C2	1.606051	0.007008	0.049527	2.696447	Up	SPATA31 subfamily C member 2
COL6A3	1.59849	2.57E-08	4.74E-06	5.56868	Up	collagen type VI alpha 3 chain
MAPK4	1.583571	0.002391	0.023885	3.0368	Up	mitogen-activated protein kinase 4
OAS2	1.57667	0.002062	0.02144	3.08113	Up	2'-5'-oligoadenylate synthetase 2
AQP7	1.564682	2.01E-05	0.000792	4.263552	Up	aquaporin 7
SLC25A48	1.563621	0.001616	0.017994	3.152948	Up	solute carrier family 25 member 48
ETV4	1.562936	0.000269	0.005148	3.643839	Up	ETS variant transcription factor 4
MAOB	1.561413	1.32E-08	2.88E-06	5.683282	Up	monoamine oxidase B
C2CD4B	1.560294	1.38E-11	9.97E-09	6.760282	Up	C2 calcium dependent domain containing 4B
CCDC178	1.555319	0.006459	0.046949	2.723504	Up	coiled-coil domain containing 178
GPC6	1.545071	0.000569	0.008694	3.445993	Up	glypican 6
KCNJ2	1.54264	0.005658	0.042973	2.766965	Up	potassium inwardly rectifying channel subfamily J member 2
OR5D14	1.535933	0.004061	0.034442	2.873396	Up	olfactory receptor family 5 subfamily D member 14
MT1E	1.527259	4.13E-05	0.001326	4.100352	Up	metallothionein 1E
SOCS5	1.523522	0.002001	0.02099	3.090019	Up	suppressor of cytokine signaling 5
GMNC	1.517516	0.001378	0.016174	3.199272	Up	geminin coiled-coil domain containing
BCL9	1.517476	6.32E-05	0.00178	4.00057	Up	BCL9 transcription coactivator
PDK3	1.516039	5.57E-05	0.001659	4.030114	Up	pyruvate dehydrogenase kinase 3
ABCC9	1.508688	3.88E-05	0.001266	4.114451	Up	ATP binding cassette subfamily C member 9
POU6F2	1.507127	0.000877	0.011878	3.327431	Up	POU class 6 homeobox 2
BTG2	1.506976	1.08E-05	0.000512	4.40043	Up	BTG anti-proliferation factor 2
A4GNT	1.487207	0.006669	0.047915	2.712924	Up	alpha-1,4-N-acetylglucosaminyltransferase
CST6	1.474865	0.005179	0.040581	2.795655	Up	cystatin E/M
CELP	1.456416	0.000752	0.010713	3.369855	Up	carboxyl ester lipase pseudogene
PRR15	1.44211	4.79E-05	0.001473	4.065781	Up	proline rich 15
VEGFC	1.439026	0.000138	0.00323	3.81237	Up	vascular endothelial growth factor C
FAM20C	1.417883	3.53E-07	3.87E-05	5.092481	Up	FAM20C golgi associated secretory pathway kinase
MPZ	1.412425	0.001225	0.015005	3.232986	Up	myelin protein zero
C16orf89	1.406088	0.002355	0.023671	3.041349	Up	chromosome 16 open reading frame 89
USP27X	1.405375	2.98E-05	0.001061	4.175094	Up	ubiquitin specific peptidase 27 X-linked
STK32B	1.401504	0.00137	0.016106	3.200934	Up	serine/threonine kinase 32B
TMEM176A	1.395841	0.001167	0.014603	3.24678	Up	transmembrane protein 176A
KLK13	1.39366	0.003137	0.028793	2.95399	Up	kallikrein related peptidase 13
RPS6	1.393238	0.000141	0.003288	3.806963	Up	ribosomal protein S6
ID3	1.379774	0.001032	0.01339	3.281721	Up	inhibitor of DNA binding 3, HLH protein

PGAP2	1.372801	0.003315	0.029859	2.936936	Up	post-GPI attachment to proteins 2
ALOXE3	1.371318	0.005208	0.040713	2.793904	Up	arachidonatelipoxygenase 3
LSM11	1.370033	0.000167	0.003679	3.763746	Up	LSM11, U7 small nuclear RNA associated
BCAP31	1.366767	0.000323	0.005863	3.596276	Up	B cell receptor associated protein 31
DDIT4	1.357877	2.95E-05	0.001054	4.177066	Up	DNA damage inducible transcript 4
DPP4	1.354505	0.000874	0.01186	3.328261	Up	dipeptidyl peptidase 4
TYSND1	1.351009	1.59E-09	5.04E-07	6.035046	Up	trypsin like peroxisomal matrix peptidase 1
IRF2BP2	1.34637	5.95E-18	2.15E-14	8.633426	Up	interferon regulatory factor 2 binding protein 2
KLF15	1.343721	1.94E-06	0.000145	4.760024	Up	Kruppel like factor 15
PCDHB7	1.334027	0.002902	0.027259	2.97794	Up	protocadherin beta 7
EGR3	1.31896	0.00597	0.044535	2.749441	Up	early growth response 3
RNF165	1.312414	0.004877	0.038959	2.815046	Up	ring finger protein 165
GRPR	1.2879	0.000461	0.007519	3.502487	Up	gastrin releasing peptide receptor
SLC10A5	1.281611	0.000367	0.006373	3.562596	Up	solute carrier family 10 member 5
AQP8	1.275576	0.000165	0.003653	3.767345	Up	aquaporin 8
SLC22A17	1.275441	0.005167	0.040504	2.796408	Up	solute carrier family 22 member 17
PHLDA1	1.265	7.26E-07	6.77E-05	4.954344	Up	pleckstrin homology like domain family A member 1
FAM86B2	1.261397	0.00011	0.002723	3.868009	Up	family with sequence similarity 86 member B2
TNXA	1.26094	0.000548	0.008447	3.456266	Up	tenascin XA (pseudogene)
LTBP4	1.249779	1.25E-10	6.48E-08	6.432767	Up	latent transforming growth factor beta binding protein 4
IKZF4	1.247809	0.005701	0.043119	2.764503	Up	IKAROS family zinc finger 4
CREB3L1	1.240081	0.001747	0.019045	3.13026	Up	cAMP responsive element binding protein 3 like 1
A1CF	1.237404	0.000302	0.00558	3.613598	Up	APOBEC1 complementation factor
EMX1	1.231921	0.007097	0.049918	2.692267	Up	empty spiracles homeobox 1
NAT10	1.230925	0.000288	0.005418	3.625785	Up	N-acetyltransferase 10
NETO2	1.226436	2.78E-05	0.001004	4.191134	Up	neuropilin and tolloid like 2
ACSL6	1.22516	0.000699	0.010166	3.390161	Up	acyl-CoA synthetase long chain family member 6
KLF3	1.222656	2.23E-09	6.52E-07	5.979866	Up	Kruppel like factor 3
ZFP36	1.222469	2.71E-07	3.23E-05	5.142302	Up	ZFP36 ring finger protein
QDPR	1.212418	0.000429	0.007144	3.521702	Up	quinoiddihydropteridinereductase
OAS1	1.211224	0.004602	0.03752	2.833639	Up	2'-5'-oligoadenylate synthetase 1
ETV5	1.20819	3.13E-06	0.00021	4.662414	Up	ETS variant transcription factor 5
GRIK5	1.206035	0.002239	0.022781	3.056565	Up	glutamate ionotropic receptor kainate type subunit 5
KL	1.201704	0.006204	0.045712	2.736802	Up	klotho
ZNF385C	1.200196	0.00318	0.029058	2.94975	Up	zinc finger protein 385C
TMEM168	1.200047	0.001202	0.014842	3.238427	Up	transmembrane protein 168
GADD45B	1.195691	6.00E-06	0.000339	4.526504	Up	growth arrest and DNA damage inducible beta
SLC29A3	1.193652	1.40E-05	0.000618	4.344205	Up	solute carrier family 29 member 3
GPR63	1.189122	5.77E-05	0.001693	4.022037	Up	G protein-coupled receptor 63
MAN1A1	1.187174	5.53E-06	0.000322	4.54348	Up	mannosidase alpha class 1A member 1
NXN	1.184622	3.38E-05	0.001161	4.146023	Up	nucleoredoxin
CGREF1	1.181501	0.004649	0.037769	2.830375	Up	cell growth regulator with EF-hand domain 1
TLE3	1.181041	1.46E-09	4.91E-07	6.048256	Up	TLE family member 3, transcriptional corepressor

RPL8	1.175798	8.84E-06	0.000445	4.443715	Up	ribosomal protein L8
HEYL	1.175375	7.83E-05	0.002098	3.94967	Up	hes related family bHLH transcription factor with YRPW motif like
PER3	1.174824	2.57E-06	0.00018	4.702617	Up	period circadian regulator 3
CXXC4	1.172558	0.000526	0.008232	3.46716	Up	CXXC finger protein 4
HRAS	1.17075	4.69E-05	0.001454	4.070447	Up	HRas proto-oncogene, GTPase
GLI3	1.168455	0.00011	0.002728	3.866542	Up	GLI family zinc finger 3
SYCN	1.16423	0.001588	0.017817	3.158183	Up	syncollin
WDR89	1.15871	0.003082	0.028428	2.959443	Up	WD repeat domain 89
KIAA0408	1.156987	0.00359	0.031565	2.912147	Up	KIAA0408
SFTPD	1.156467	0.000869	0.011855	3.329763	Up	surfactant protein D
MYC	1.155459	0.000232	0.004664	3.68131	Up	MYC proto-oncogene, bHLH transcription factor
TTI1	1.153438	7.67E-06	0.000403	4.474283	Up	TELO2 interacting protein 1
IFIT3	1.153223	0.001484	0.017069	3.177774	Up	interferon induced protein with tetratricopeptide repeats 3
IGSF8	1.147182	3.42E-05	0.00117	4.143533	Up	immunoglobulin superfamily member 8
RPRD2	1.136951	4.05E-09	1.04E-06	5.882334	Up	regulation of nuclear pre-mRNA domain containing 2
MT1JP	1.135989	0.002674	0.025796	3.002974	Up	metallothionein 1J, pseudogene
SNORA81	1.134404	7.05E-05	0.001942	3.974527	Up	small nucleolar RNA, H/ACA box 81
DMD	1.134394	0.0025	0.024649	3.02331	Up	dystrophin
ZNF416	1.12885	3.44E-06	0.00022	4.642339	Up	zinc finger protein 416
AQP12B	1.122447	0.003687	0.032134	2.903728	Up	aquaporin 12B
FKBP8	1.12091	0.000337	0.006069	3.585204	Up	FKBP prolylisomerase 8
IRS1	1.109776	2.50E-09	7.07E-07	5.961342	Up	insulin receptor substrate 1
KIAA1958	1.104138	2.20E-07	2.72E-05	5.181865	Up	KIAA1958
RPS28	1.099636	2.86E-10	1.25E-07	6.306441	Up	ribosomal protein S28
TMEM140	1.093078	0.00016	0.003573	3.774447	Up	transmembrane protein 140
DBP	1.092264	1.15E-06	9.80E-05	4.86439	Up	D-box binding PAR bZIP transcription factor
MUC6	1.08831	0.005474	0.041981	2.777718	Up	mucin 6, oligomeric mucus/gel-forming
MTCH1	1.088002	0.004192	0.035182	2.86336	Up	mitochondrial carrier 1
CHST10	1.086677	0.005118	0.040291	2.799519	Up	carbohydrate sulfotransferase 10
ABHD15	1.086125	0.000312	0.005712	3.605158	Up	abhydrolase domain containing 15
KLF9	1.080005	8.43E-13	9.53E-10	7.15394	Up	Kruppel like factor 9
EIF4B	1.06405	0.000817	0.011276	3.347136	Up	eukaryotic translation initiation factor 4B
KLF10	1.055746	0.000299	0.005546	3.616276	Up	Kruppel like factor 10
PODXL	1.05305	1.75E-06	0.000137	4.780037	Up	podocalyxin like
BVES	1.050529	0.000813	0.011258	3.348218	Up	blood vessel epicardial substance
GLTP	1.050372	5.80E-06	0.000333	4.533591	Up	glycolipid transfer protein
MNT	1.045232	2.72E-05	0.000992	4.195389	Up	MAX network transcriptional repressor
LSR	1.044877	1.76E-05	0.000726	4.292801	Up	lipolysis stimulated lipoprotein receptor
CEL	1.038816	0.002503	0.024649	3.023013	Up	carboxyl ester lipase
NUP205	1.036199	0.002925	0.027371	2.975558	Up	nucleoporin 205
MT1L	1.036012	0.001676	0.018469	3.142292	Up	metallothionein 1L, pseudogene
FOSL2	1.035358	3.00E-05	0.001065	4.173687	Up	FOS like 2, AP-1 transcription factor subunit
ACVR2B-AS1	1.03269	0.002713	0.026028	2.998466	Up	ACVR2B antisense RNA 1

SLC1A5	1.032611	0.000353	0.006238	3.572762	Up	solute carrier family 1 member 5
ZNF362	1.03072	5.17E-06	0.000306	4.557695	Up	zinc finger protein 362
WASF1	1.029075	9.96E-05	0.002531	3.891542	Up	WASP family member 1
PAPSS2	1.024653	0.003229	0.029385	2.945045	Up	3'-phosphoadenosine 5'-phosphosulfate synthase 2
TMCO4	1.023584	0.000267	0.005139	3.645801	Up	transmembrane and coiled-coil domains 4
KIAA1549	1.022711	0.000159	0.003558	3.777019	Up	KIAA1549
NR1D1	1.022533	0.002444	0.024264	3.030221	Up	nuclear receptor subfamily 1 group D member 1
DUSP4	1.013696	5.02E-05	0.001535	4.054499	Up	dual specificity phosphatase 4
SNX19	1.013619	3.95E-05	0.001287	4.110135	Up	sorting nexin 19
SMCR8	1.013255	1.35E-05	0.000604	4.351545	Up	SMCR8-C9orf72 complex subunit
FECH	1.008972	1.98E-05	0.000786	4.267423	Up	ferrochelatase
FOXN3	1.007664	3.12E-10	1.31E-07	6.292462	Up	forkhead box N3
IL6ST	1.006029	0.002468	0.024433	3.027296	Up	interleukin 6 signal transducer
IL6R	0.999744	0.006884	0.048917	2.702392	Up	interleukin 6 receptor
PCDHB6	0.994986	0.005158	0.040486	2.796974	Up	protocadherin beta 6
ZNF581	0.993708	0.000106	0.00265	3.876665	Up	zinc finger protein 581
KLF6	0.991792	6.78E-07	6.43E-05	4.967609	Up	Kruppel like factor 6
CPA1	0.99028	0.003622	0.031696	2.909338	Up	carboxypeptidase A1
ABCA1	0.989596	0.000135	0.003174	3.817307	Up	ATP binding cassette subfamily A member 1
ZFP36L1	0.983112	0.000597	0.009015	3.432766	Up	ZFP36 ring finger protein like 1
PBX1	0.979927	4.02E-13	5.59E-10	7.254949	Up	PBX homeobox 1
DYSF	0.977559	0.006334	0.046301	2.729951	Up	dysferlin
SH3RF1	0.977474	0.000206	0.004295	3.711432	Up	SH3 domain containing ring finger 1
PLEKHG6	0.975335	0.000311	0.0057	3.605994	Up	pleckstrin homology and RhoGEF domain containing G6
URM1	0.974945	1.43E-08	3.05E-06	5.670336	Up	ubiquitin related modifier 1
ERN1	0.974217	0.000112	0.002749	3.86398	Up	endoplasmic reticulum to nucleus signaling 1
RPL18	0.972875	1.59E-06	0.000129	4.799987	Up	ribosomal protein L18
CNTN3	0.966787	0.001627	0.018064	3.151099	Up	contactin 3
CYGB	0.960228	4.03E-05	0.001303	4.105482	Up	cytoglobin
RNF24	0.952932	0.000767	0.010872	3.364507	Up	ring finger protein 24
ABCG2	0.942728	0.002598	0.025251	3.011741	Up	ATP binding cassette subfamily G member 2 (Junior blood group)
PRRC1	0.940958	1.44E-05	0.000633	4.337711	Up	proline rich coiled-coil 1
NHEJ1	0.940305	0.005191	0.040636	2.794938	Up	non-homologous end joining factor 1
PDK2	0.936816	1.05E-05	0.000505	4.406224	Up	pyruvate dehydrogenase kinase 2
BOC	0.933366	6.19E-06	0.000345	4.519766	Up	BOC cell adhesion associated, oncogene regulated
PNPLA4	0.92827	1.98E-09	6.00E-07	5.999168	Up	patatin like phospholipase domain containing 4
SELENBP1	0.925116	5.37E-07	5.49E-05	5.012682	Up	selenium binding protein 1
STAT1	0.92016	2.19E-08	4.26E-06	5.596302	Up	signal transducer and activator of transcription 1
TMC4	0.918004	7.50E-06	0.000396	4.479012	Up	transmembrane channel like 4
HSPA2	0.917681	0.000234	0.004701	3.678748	Up	heat shock protein family A (Hsp70) member 2
DUSP1	0.916798	6.01E-06	0.000339	4.526156	Up	dual specificity phosphatase 1
CLSTN2	0.915169	0.000756	0.010747	3.368549	Up	calsyntenin 2
DIP2B	0.914675	3.23E-05	0.001126	4.156545	Up	disco interacting protein 2 homolog B

FMOD	0.902186	0.001186	0.01473	3.242196	Up	fibromodulin
SNORA46	0.900951	0.006185	0.045618	2.737784	Up	small nucleolar RNA, H/ACA box 46
MYADM	0.899156	9.01E-06	0.000447	4.439634	Up	myeloid associated differentiation marker
ARPC1A	0.896149	8.17E-09	1.92E-06	5.764985	Up	actin related protein 2/3 complex subunit 1A
PCDHB11	0.894232	0.006266	0.045933	2.733512	Up	protocadherin beta 11
KCTD12	0.89297	0.000774	0.010938	3.361758	Up	potassium channel tetramerization domain containing 12
APOD	0.89142	0.00345	0.030622	2.924542	Up	apolipoprotein D
GLS	0.884954	0.00026	0.00507	3.652426	Up	glutaminase
FBXO32	0.881866	3.15E-06	0.000211	4.660468	Up	F-box protein 32
ST6GALNAC6	0.879554	2.07E-05	0.000809	4.257572	Up	ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 6
SRM	0.878308	0.000309	0.005677	3.607559	Up	spermidine synthase
DIRAS3	0.876306	0.003122	0.028685	2.955463	Up	DIRAS family GTPase 3
NR0B2	0.874431	7.41E-05	0.002024	3.962782	Up	nuclear receptor subfamily 0 group B member 2
NHS	0.87443	0.005302	0.041077	2.788104	Up	NHS actin remodeling regulator
SYVN1	0.872096	0.000139	0.003248	3.810686	Up	synoviolin 1
ARL6IP1	0.872037	0.001505	0.017219	3.173755	Up	ADP ribosylation factor like GTPase 6 interacting protein 1
TCF7L2	0.871267	8.46E-06	0.000435	4.45327	Up	transcription factor 7 like 2
TMUB1	0.869907	2.94E-05	0.00105	4.178279	Up	transmembrane and ubiquitin like domain containing 1
SNHG9	0.868128	0.000191	0.004072	3.730146	Up	small nucleolar RNA host gene 9
DHRS11	0.86627	5.84E-08	9.11E-06	5.423684	Up	dehydrogenase/reductase 11
MRPL37	0.864054	1.60E-06	0.000129	4.79874	Up	mitochondrial ribosomal protein L37
DLL4	0.858948	0.003304	0.029823	2.937894	Up	delta like canonical Notch ligand 4
HELZ2	0.856157	8.62E-05	0.002263	3.926561	Up	helicase with zinc finger 2
NNMT	0.851608	0.001206	0.014883	3.237453	Up	nicotinamide N-methyltransferase
SMAD1	0.850932	1.92E-07	2.46E-05	5.206868	Up	SMAD family member 1
TP53	0.850773	0.000201	0.004226	3.717618	Up	tumor protein p53
PCDH18	0.850737	0.000247	0.004858	3.665575	Up	protocadherin 18
FAM160B2	0.848165	0.00339	0.030322	2.929974	Up	family with sequence similarity 160 member B2
ELK1	0.84679	7.59E-05	0.002058	3.957072	Up	ETS transcription factor ELK1
SUN2	0.846146	4.47E-08	7.36E-06	5.471101	Up	Sad1 and UNC84 domain containing 2
TMEM150A	0.84345	7.57E-07	6.88E-05	4.946241	Up	transmembrane protein 150A
PTBP1	0.84235	1.45E-05	0.000636	4.335712	Up	polypyrimidine tract binding protein 1
SOS1	0.842032	1.25E-05	0.000573	4.369507	Up	SOS Ras/Rac guanine nucleotide exchange factor 1
PRKACA	0.841424	0.000208	0.004333	3.708612	Up	protein kinase cAMP-activated catalytic subunit alpha
BACH2	0.840276	0.004124	0.034884	2.868539	Up	BTB domain and CNC homolog 2
TOR2A	0.838785	0.000805	0.011164	3.351168	Up	torsin family 2 member A
CTSF	0.836129	6.47E-06	0.000355	4.51037	Up	cathepsin F
EGFR	0.835307	0.002303	0.023314	3.048103	Up	epidermal growth factor receptor
ETS1	0.834376	0.002812	0.0267	2.987581	Up	ETS proto-oncogene 1, transcription factor
PIK3CA	0.834263	9.81E-06	0.000476	4.421306	Up	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha
ZNRF1	0.834005	0.000348	0.006201	3.57648	Up	zinc and ring finger 1
CMPK2	0.833442	0.000382	0.006568	3.552511	Up	cytidine/uridine monophosphate kinase 2
C17orf49	0.831035	6.49E-08	9.94E-06	5.404842	Up	chromosome 17 open reading frame 49

GUK1	0.830906	0.005863	0.043941	2.755329	Up	guanylate kinase 1
TSHZ1	0.830001	0.001412	0.016467	3.192239	Up	teashirt zinc finger homeobox 1
ZNF326	0.829871	2.09E-05	0.000816	4.255297	Up	zinc finger protein 326
MED13L	0.825296	1.99E-05	0.000788	4.266458	Up	mediator complex subunit 13L
GCNT2	0.824275	0.006687	0.047973	2.712061	Up	glucosaminyl (N-acetyl) transferase 2 (I blood group)
SAE1	0.821934	1.76E-05	0.000726	4.292772	Up	SUMO1 activating enzyme subunit 1
GTPBP8	0.820509	1.28E-06	0.000107	4.842977	Up	GTP binding protein 8 (putative)
PKN1	0.820314	9.18E-05	0.002377	3.911368	Up	protein kinase N1
TNFRSF1A	0.819517	8.65E-06	0.000442	4.448543	Up	TNF receptor superfamily member 1A
ELOVL1	0.818479	2.24E-06	0.000163	4.730554	Up	ELOVL fatty acid elongase 1
TUT1	0.81736	0.000101	0.002556	3.887148	Up	terminal uridylyltransferase 1, U6 snRNA-specific
NCSTN	0.814539	5.60E-10	2.16E-07	6.201177	Up	nicastrin
MFAP2	0.814276	0.004538	0.037128	2.838125	Up	microfibril associated protein 2
YBX1	0.812937	9.16E-05	0.002377	3.911852	Up	Y-box binding protein 1
PPP1R3B	0.810696	0.000614	0.009215	3.425208	Up	protein phosphatase 1 regulatory subunit 3B
PLCE1	0.80763	0.005261	0.040902	2.790596	Up	phospholipase C epsilon 1
NDST1	0.801304	1.38E-10	6.95E-08	6.417856	Up	N-deacetylase and N-sulfotransferase 1
KCNJ8	0.800647	0.000248	0.004871	3.664642	Up	potassium inwardly rectifying channel subfamily J member 8
ATF6B	0.795539	5.53E-06	0.000322	4.543457	Up	activating transcription factor 6 beta
GAMT	0.794851	0.000283	0.00535	3.630634	Up	guanidinoacetate N-methyltransferase
DGCR2	0.792202	0.000263	0.005112	3.649418	Up	DiGeorge syndrome critical region gene 2
ME2	0.792173	0.002342	0.02356	3.043104	Up	malic enzyme 2
SNORA70F	0.791991	0.001262	0.015252	3.22447	Up	small nucleolar RNA, H/ACA box 70F
TPI1	0.791213	0.000701	0.010178	3.389207	Up	triosephosphateisomerase 1
JMJD8	0.790139	3.01E-05	0.001068	4.172555	Up	jumonji domain containing 8
NES	0.788137	1.56E-05	0.000667	4.320476	Up	nestin
CDC42EP3	0.787657	0.006527	0.047324	2.72008	Up	CDC42 effector protein 3
SECISBP2L	0.785942	0.002747	0.026216	2.994768	Up	SECIS binding protein 2 like
PRPF8	0.785467	4.09E-05	0.001317	4.102281	Up	pre-mRNA processing factor 8
DNAJC4	0.784209	1.19E-06	0.000101	4.856749	Up	DnaJ heat shock protein family (Hsp40) member C4
EIF3B	0.783198	4.65E-05	0.001445	4.072672	Up	eukaryotic translation initiation factor 3 subunit B
EPHX1	0.78283	0.000166	0.003661	3.766555	Up	epoxide hydrolase 1
WDTC1	0.782558	8.41E-06	0.000434	4.454475	Up	WD and tetratricopeptide repeats 1
MAML1	0.78192	2.54E-05	0.000933	4.210975	Up	mastermind like transcriptional coactivator 1
PCDHB4	0.779944	0.00151	0.01726	3.172676	Up	protocadherin beta 4
CRNKL1	0.776112	0.001354	0.015976	3.204332	Up	crooked neck pre-mRNA splicing factor 1
NFIB	0.775622	0.005204	0.040705	2.794109	Up	nuclear factor I B
MAPK3	0.774729	6.63E-06	0.000361	4.505204	Up	mitogen-activated protein kinase 3
SLC23A2	0.771981	0.005612	0.042695	2.769626	Up	solute carrier family 23 member 2
RPL18A	0.771037	0.000204	0.004258	3.713912	Up	ribosomal protein L18a
FAM83B	0.769782	0.000435	0.007223	3.51776	Up	family with sequence similarity 83 member B
CNDP2	0.768381	0.000586	0.008901	3.43821	Up	carnosinedipeptidase 2
SERTAD2	0.768202	3.98E-05	0.001293	4.108585	Up	SERTA domain containing 2

RCE1	0.76665	0.000172	0.003741	3.757149	Up	Ras converting CAAX endopeptidase 1
C2orf69	0.766464	8.05E-05	0.002142	3.942914	Up	chromosome 2 open reading frame 69
FOXK1	0.764006	0.001585	0.0178	3.158636	Up	forkhead box K1
ZNF646	0.763811	0.000536	0.00834	3.462129	Up	zinc finger protein 646
CAMSAP3	0.762877	1.95E-05	0.000779	4.271089	Up	calmodulin regulated spectrin associated protein family member 3
ACVR2B	0.761578	2.49E-05	0.000919	4.215416	Up	activin A receptor type 2B
ATXN7L1	0.761216	0.001983	0.020842	3.09281	Up	ataxin 7 like 1
LRRC8B	0.761015	0.000468	0.007577	3.49819	Up	leucine rich repeat containing 8 VRAC subunit B
PLOD3	0.760059	3.88E-05	0.001266	4.114231	Up	procollagen-lysine,2-oxoglutarate 5-dioxygenase 3
FAM193B	0.758019	1.78E-05	0.000726	4.291384	Up	family with sequence similarity 193 member B
ZFHX3	0.757752	0.001036	0.013414	3.280609	Up	zinc finger homeobox 3
SMURF1	0.756591	1.06E-05	0.000508	4.404419	Up	SMAD specific E3 ubiquitin protein ligase 1
AOX1	0.756086	0.003594	0.031565	2.911801	Up	aldehyde oxidase 1
RPS15	0.755554	6.99E-07	6.59E-05	4.961597	Up	ribosomal protein S15
PRMT6	0.753247	0.001239	0.01511	3.22983	Up	protein arginine methyltransferase 6
TRIM24	0.752928	1.16E-05	0.000543	4.384086	Up	tripartite motif containing 24
PRKCSH	0.750891	0.000284	0.005365	3.629653	Up	protein kinase C substrate 80K-H
ETV6	0.75061	9.73E-07	8.46E-05	4.896989	Up	ETS variant transcription factor 6
GSK3A	0.7503	0.000194	0.004091	3.727348	Up	glycogen synthase kinase 3 alpha
WDR74	0.749277	0.000605	0.009092	3.429532	Up	WD repeat domain 74
KCNC4	0.746517	0.002407	0.023989	3.03483	Up	potassium voltage-gated channel subfamily C member 4
LARP6	0.745789	7.94E-05	0.002124	3.946332	Up	La ribonucleoprotein 6, translational regulator
BCOR	0.744144	0.00012	0.002934	3.845436	Up	BCL6 corepressor
PSD4	0.741924	0.005215	0.040726	2.793473	Up	pleckstrin and Sec7 domain containing 4
URB1	0.74192	6.05E-05	0.00174	4.01084	Up	URB1 ribosome biogenesis homolog
RAB4A	0.740681	0.000763	0.010829	3.365815	Up	RAB4A, member RAS oncogene family
ZNF341	0.740369	0.002638	0.025544	3.007083	Up	zinc finger protein 341
SGTA	0.740279	0.000162	0.003593	3.77241	Up	small glutamine rich tetratricopeptide repeat containing alpha
STUB1	0.739139	0.000973	0.012833	3.298143	Up	STIP1 homology and U-box containing protein 1
SLC35E1	0.736682	9.91E-09	2.30E-06	5.732304	Up	solute carrier family 35 member E1
RSBN1	0.73582	4.22E-08	7.07E-06	5.481284	Up	round spermatid basic protein 1
NPAS2	0.732705	3.23E-05	0.001126	4.156955	Up	neuronal PAS domain protein 2
MAOA	0.731781	4.31E-06	0.000262	4.595946	Up	monoamine oxidase A
USP1	0.728983	0.003174	0.029017	2.950339	Up	ubiquitin specific peptidase 1
RBM47	0.728968	1.56E-08	3.21E-06	5.654557	Up	RNA binding motif protein 47
RNF43	0.728384	0.000997	0.013032	3.291369	Up	ring finger protein 43
KIAA0930	0.728341	6.95E-05	0.001924	3.977861	Up	KIAA0930
SHISA5	0.72744	0.000573	0.008736	3.444214	Up	shisa family member 5
TCOF1	0.727002	0.00054	0.008367	3.460175	Up	treacle ribosome biogenesis factor 1
NCL	0.725941	0.002185	0.022354	3.063829	Up	nucleolin
FKBP5	0.724631	7.85E-06	0.000411	4.469326	Up	FKBP prolylisomerase 5
RBM22	0.723796	3.19E-06	0.000211	4.6585	Up	RNA binding motif protein 22
SLC48A1	0.720957	2.30E-05	0.000874	4.233151	Up	solute carrier family 48 member 1

GNL1	0.720727	0.000309	0.005676	3.607864	Up	G protein nucleolar 1 (putative)
FOXP1	0.720205	1.58E-09	5.04E-07	6.036016	Up	forkhead box P1
TRAPPC3	0.719608	0.000551	0.008489	3.45471	Up	trafficking protein particle complex 3
METTL14	0.718111	0.000565	0.008669	3.447662	Up	methyltransferase like 14
PIGM	0.716435	0.000194	0.004091	3.727242	Up	phosphatidylinositol glycan anchor biosynthesis class M
MZT2B	0.714175	0.001677	0.018471	3.142085	Up	mitotic spindle organizing protein 2B
ATF7IP	0.712488	4.27E-09	1.07E-06	5.873211	Up	activating transcription factor 7 interacting protein
RWDD2B	0.711793	0.000232	0.00466	3.681821	Up	RWD domain containing 2B
POLR1D	0.708737	0.005643	0.042875	2.767845	Up	RNA polymerase I and III subunit D
UBIAD1	0.706576	8.09E-06	0.00042	4.46291	Up	UbiAprenyltransferase domain containing 1
SFXN2	0.700426	0.001682	0.018509	3.141299	Up	sideroflexin 2
FIGN	0.699523	3.68E-05	0.001226	4.126718	Up	fidgetin, microtubule severing factor
UBAP2	0.699319	3.77E-08	6.56E-06	5.50114	Up	ubiquitin associated protein 2
UBE2E2	0.699156	5.75E-05	0.001693	4.022695	Up	ubiquitin conjugating enzyme E2 E2
MX1	0.698814	0.003319	0.029859	2.936555	Up	MX dynamin like GTPase 1
SPPL3	0.697852	0.000696	0.010145	3.390959	Up	signal peptide peptidase like 3
KCTD11	0.697791	2.01E-05	0.000792	4.263333	Up	potassium channel tetramerization domain containing 11
HSP90AA1	0.696743	0.00019	0.00406	3.731557	Up	heat shock protein 90 alpha family class A member 1
BTG1	0.694132	4.22E-06	0.000257	4.600208	Up	BTG anti-proliferation factor 1
GALM	0.693238	0.005154	0.040486	2.797233	Up	galactosemutarotase
GAB1	0.693194	1.58E-08	3.21E-06	5.652613	Up	GRB2 associated binding protein 1
PXMP2	0.692523	0.001283	0.015424	3.21973	Up	peroxisomal membrane protein 2
SCARNA17	0.691261	8.34E-06	0.000432	4.456247	Up	small Cajal body-specific RNA 17
S1PR1	0.691074	6.64E-05	0.001855	3.988707	Up	sphingosine-1-phosphate receptor 1
THRB	0.691029	0.000885	0.011987	3.324668	Up	thyroid hormone receptor beta
RPL39	0.690209	0.005561	0.042488	2.77258	Up	ribosomal protein L39
UTP14A	0.6899	0.003424	0.030472	2.926834	Up	UTP14A small subunit processome component
EDNRB	0.689734	0.000237	0.004752	3.6754	Up	endothelin receptor type B
CRTC3	0.689519	8.27E-05	0.002191	3.936548	Up	CREB regulated transcription coactivator 3
AK1	0.689426	0.001162	0.014574	3.248124	Up	adenylate kinase 1
PTGER3	0.687494	0.001956	0.020638	3.09677	Up	prostaglandin E receptor 3
SYBU	0.687308	0.000239	0.004773	3.674039	Up	syntabulin
MED25	0.687197	0.002406	0.023989	3.034873	Up	mediator complex subunit 25
ERP29	0.686161	0.000267	0.005139	3.645521	Up	endoplasmic reticulum protein 29
RBM23	0.685812	0.000216	0.004436	3.699217	Up	RNA binding motif protein 23
GPATCH4	0.684195	0.001189	0.014747	3.241437	Up	G-patch domain containing 4
CDNF	0.684189	0.001318	0.015708	3.212028	Up	cerebral dopamine neurotrophic factor
RNASEK	0.683852	0.005382	0.041449	2.783259	Up	ribonuclease K
LPCAT3	0.683539	0.000328	0.005946	3.591945	Up	lysophosphatidylcholineacyltransferase 3
CASC3	0.683245	0.000342	0.006117	3.581073	Up	CASC3 exon junction complex subunit
MTMR3	0.682235	0.000873	0.01186	3.328634	Up	myotubularin related protein 3
TNKS	0.681959	0.000955	0.012674	3.303437	Up	tankyrase
SF3A1	0.681792	0.000107	0.002666	3.87484	Up	splicing factor 3a subunit 1

CHID1	0.681692	2.35E-05	0.000888	4.228751	Up	chitinase domain containing 1
AGPAT3	0.679929	4.02E-06	0.000249	4.610538	Up	1-acylglycerol-3-phosphate O-acyltransferase 3
ADPRHL1	0.67793	0.003299	0.029823	2.93839	Up	ADP-ribosylhydrolase like 1
MEX3C	0.676707	1.74E-07	2.28E-05	5.225485	Up	mex-3 RNA binding family member C
SIAH2	0.676628	4.59E-05	0.001437	4.075423	Up	siah E3 ubiquitin protein ligase 2
ACD	0.674822	0.000397	0.006739	3.541993	Up	ACD shelterin complex subunit and telomerase recruitment factor
NFKBIA	0.671989	2.49E-09	7.07E-07	5.961923	Up	NFKB inhibitor alpha
CDC42EP4	0.670577	3.53E-05	0.001193	4.136046	Up	CDC42 effector protein 4
ARHGAP17	0.670458	0.000353	0.006238	3.572609	Up	Rho GTPase activating protein 17
GJA1	0.669532	0.000191	0.004071	3.730543	Up	gap junction protein alpha 1
RNPS1	0.669286	0.000469	0.007577	3.498063	Up	RNA binding protein with serine rich domain 1
ATP13A2	0.668974	0.001969	0.020738	3.094808	Up	ATPase cation transporting 13A2
ZSWIM3	0.666665	0.005783	0.043574	2.759838	Up	zinc finger SWIM-type containing 3
TXNDC5	0.666561	6.22E-05	0.001775	4.004346	Up	thioredoxin domain containing 5
PPFIBP2	0.66328	0.00471	0.038127	2.826221	Up	PPFIA binding protein 2
MRPL49	0.661083	4.76E-05	0.001473	4.066891	Up	mitochondrial ribosomal protein L49
SLC35C2	0.660269	0.002623	0.025458	3.008774	Up	solute carrier family 35 member C2
CD34	0.656903	0.001941	0.020527	3.099122	Up	CD34 molecule
SQSTM1	0.656832	0.000903	0.012146	3.319117	Up	sequestosome 1
DEAF1	0.656044	0.000482	0.007723	3.490807	Up	DEAF1 transcription factor
CPNE8	0.655935	0.006745	0.048175	2.709168	Up	copine 8
INSR	0.655878	0.001522	0.017355	3.170368	Up	insulin receptor
RPL19	0.655743	0.0001	0.002543	3.889412	Up	ribosomal protein L19
NR1D2	0.655727	0.001279	0.015407	3.220621	Up	nuclear receptor subfamily 1 group D member 2
SLC25A43	0.655559	0.000873	0.01186	3.32843	Up	solute carrier family 25 member 43
AGBL5	0.654572	0.003824	0.032915	2.892293	Up	ATP/GTP binding protein like 5
SLC39A4	0.653952	0.005292	0.041019	2.788697	Up	solute carrier family 39 member 4
SP2	0.652169	0.002758	0.026271	2.993532	Up	Sp2 transcription factor
SLC2A4RG	0.65117	0.00165	0.018241	3.146991	Up	SLC2A4 regulator
YIPF3	0.650173	3.26E-05	0.001131	4.15422	Up	Yip1 domain family member 3
MRPS18B	0.649811	7.15E-06	0.000383	4.489106	Up	mitochondrial ribosomal protein S18B
NEDD9	0.648825	0.000492	0.007837	3.485031	Up	neural precursor cell expressed, developmentally down-regulated 9
GADD45G	0.648736	0.006811	0.048569	2.705943	Up	growth arrest and DNA damage inducible gamma
ZNRF3	0.648723	0.001296	0.015533	3.216764	Up	zinc and ring finger 3
MAST3	0.648387	0.001533	0.017433	3.168306	Up	microtubule associated serine/threonine kinase 3
SNX12	0.648357	0.001185	0.014729	3.242554	Up	sorting nexin 12
TMED5	0.647804	4.52E-05	0.001421	4.079333	Up	transmembrane p24 trafficking protein 5
BAZ2A	0.647031	0.000218	0.004449	3.69755	Up	bromodomain adjacent to zinc finger domain 2A
CCDC86	0.646936	0.000592	0.008966	3.435136	Up	coiled-coil domain containing 86
MBOAT7	0.644983	0.005086	0.040095	2.801514	Up	membrane bound O-acyltransferase domain containing 7
GID8	0.644926	0.00015	0.003436	3.790262	Up	GID complex subunit 8 homolog
DCPS	0.642919	0.002036	0.021241	3.084943	Up	decapping enzyme, scavenger
LIG3	0.642442	5.43E-05	0.001633	4.036185	Up	DNA ligase 3

BSG	0.641779	0.001141	0.014369	3.253151	Up	basigin (Ok blood group)
SP4	0.640664	0.000992	0.012988	3.292727	Up	Sp4 transcription factor
KLF11	0.63968	1.52E-05	0.000659	4.325257	Up	Kruppel like factor 11
CIZ1	0.63856	1.87E-05	0.000756	4.279502	Up	CDKN1A interacting zinc finger protein 1
LNX1	0.636517	1.47E-05	0.000641	4.333615	Up	ligand of numb-protein X 1
RALB	0.63579	3.37E-06	0.000219	4.646621	Up	RAS like proto-oncogene B
BTF3	0.632977	0.000199	0.004195	3.720016	Up	basic transcription factor 3
ZNF836	0.632392	0.002077	0.021526	3.078926	Up	zinc finger protein 836
NET1	0.631653	0.005749	0.043387	2.761785	Up	neuroepithelial cell transforming 1
IAPP	-10.801	2.63E-45	2.38E-41	-14.126	Down	islet amyloid polypeptide
INS	-10.3513	7.60E-52	1.37E-47	-15.1498	Down	insulin
HAPLN4	-6.9522	3.78E-09	1.00E-06	-5.89366	Down	hyaluronan and proteoglycan link protein 4
ADCYAP1	-6.37952	7.01E-16	1.81E-12	-8.07029	Down	adenylatecyclase activating polypeptide 1
CSNK1G1	-6.37349	5.07E-14	8.34E-11	-7.53001	Down	casein kinase 1 gamma 1
MAFA	-6.08612	2.10E-12	1.90E-09	-7.02742	Down	MAF bZIP transcription factor A
IGLL5	-5.95682	0.00111	0.014081	-3.26108	Down	immunoglobulin lambda like polypeptide 5
WSCD2	-5.89111	1.55E-09	5.04E-07	-6.03927	Down	WSC domain containing 2
PLCH2	-5.70065	1.54E-15	3.49E-12	-7.9734	Down	phospholipase C eta 2
SLCO1A2	-5.65472	9.18E-05	0.002377	-3.9112	Down	solute carrier organic anion transporter family member 1A2
HHATL	-5.54001	4.92E-11	3.23E-08	-6.57335	Down	hedgehog acyltransferase like
DMBT1	-5.11154	0.000502	0.007945	-3.47993	Down	deleted in malignant brain tumors 1
RGS16	-4.81121	1.53E-18	9.23E-15	-8.78743	Down	regulator of G protein signaling 16
PREX1	-4.79312	5.00E-11	3.23E-08	-6.57103	Down	phosphatidylinositol-3,4,5-trisphosphate dependent Rac exchange factor 1
SYT16	-4.64825	1.25E-08	2.80E-06	-5.69211	Down	synaptotagmin 16
ASB9	-4.60995	1.08E-17	3.26E-14	-8.56492	Down	ankyrin repeat and SOCS box containing 9
LRFN2	-4.54487	1.77E-05	0.000726	-4.29175	Down	leucine rich repeat and fibronectin type III domain containing 2
NRG3	-4.53264	3.24E-05	0.001126	-4.15624	Down	neuregulin 3
HSD17B13	-4.51785	1.90E-09	5.93E-07	-6.00595	Down	hydroxysteroid 17-beta dehydrogenase 13
DLK1	-4.43907	2.20E-12	1.90E-09	-7.02104	Down	delta like non-canonical Notch ligand 1
LOC100286922	-4.09518	0.00035	0.00622	-3.57543	Down	DnaJ heat shock protein family (Hsp40) member B3 pseudogene
LRRTM3	-4.05763	3.63E-06	0.00023	-4.63163	Down	leucine rich repeat transmembrane neuronal 3
GABRA2	-3.9965	1.21E-06	0.000101	-4.85468	Down	gamma-aminobutyric acid type A receptor subunit alpha2
GTSF1	-3.96587	8.59E-06	0.00044	-4.44996	Down	gametocyte specific factor 1
NTNG2	-3.89902	1.78E-07	2.30E-05	-5.22131	Down	netrin G2
GLRA1	-3.83003	4.47E-05	0.001413	-4.08161	Down	glycine receptor alpha 1
DGKG	-3.7646	8.17E-13	9.53E-10	-7.15833	Down	diacylglycerol kinase gamma
ISX	-3.75152	0.001191	0.014761	-3.24097	Down	intestine specific homeobox
OR10J3	-3.70449	1.79E-06	0.000139	-4.77542	Down	olfactory receptor family 10 subfamily J member 3
SLC6A17	-3.70444	1.83E-05	0.00074	-4.28474	Down	solute carrier family 6 member 17
DACH2	-3.67639	4.10E-08	6.95E-06	-5.48656	Down	dachshund family transcription factor 2
VPREB1	-3.6609	0.001658	0.018315	-3.14545	Down	V-set pre-B cell surrogate light chain 1
RXRG	-3.64353	3.01E-06	0.000204	-4.67042	Down	retinoid X receptor gamma
IFNA16	-3.63676	0.00089	0.012039	-3.32325	Down	interferon alpha 16

G6PC2	-3.62269	3.42E-06	0.00022	-4.64385	Down	glucose-6-phosphatase catalytic subunit 2
OR4F5	-3.59416	0.001252	0.015226	-3.22678	Down	olfactory receptor family 4 subfamily F member 5
SLC18A2	-3.57954	7.56E-09	1.80E-06	-5.77806	Down	solute carrier family 18 member A2
BIRC8	-3.56786	5.34E-05	0.001609	-4.04035	Down	baculoviral IAP repeat containing 8
KLHL1	-3.55633	6.13E-05	0.001753	-4.00789	Down	kelch like family member 1
SLC26A9	-3.53742	0.000256	0.005002	-3.65613	Down	solute carrier family 26 member 9
OR6C74	-3.52371	0.000373	0.006457	-3.55827	Down	olfactory receptor family 6 subfamily C member 74
DKK4	-3.51465	3.70E-05	0.001229	-4.12522	Down	dickkopf WNT signaling pathway inhibitor 4
UNC5A	-3.5005	3.25E-06	0.000214	-4.65467	Down	unc-5 netrin receptor A
OR5L1	-3.49176	0.000203	0.004248	-3.71483	Down	olfactory receptor family 5 subfamily L member 1
LOC154761	-3.48046	1.69E-05	0.000707	-4.30203	Down	family with sequence similarity 115, member C pseudogene
OR4D2	-3.47937	0.001687	0.018539	-3.14047	Down	olfactory receptor family 4 subfamily D member 2
KCNG3	-3.45067	5.90E-07	5.87E-05	-4.99431	Down	potassium voltage-gated channel modifier subfamily G member 3
ARHGEF35	-3.42973	0.00378	0.032645	-2.89592	Down	Rho guanine nucleotide exchange factor 35
SLC27A6	-3.42698	0.00025	0.004903	-3.66238	Down	solute carrier family 27 member 6
OR2T33	-3.40998	0.000418	0.007022	-3.52868	Down	olfactory receptor family 2 subfamily T member 33
KIF4B	-3.39216	0.000503	0.00795	-3.47931	Down	kinesin family member 4B
CLDN25	-3.35937	0.000658	0.009732	-3.40632	Down	claudin 25
OR2T6	-3.33501	0.000203	0.004248	-3.71558	Down	olfactory receptor family 2 subfamily T member 6
EBLN1	-3.32606	0.000711	0.010271	-3.38516	Down	endogenous Bornavirus like nucleoprotein 1
TKTL2	-3.32283	0.000899	0.012131	-3.32029	Down	transketolase like 2
ST8SIA5	-3.29995	9.50E-05	0.002441	-3.90304	Down	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 5
ADAM30	-3.29013	0.003501	0.030982	-2.91998	Down	ADAM metallopeptidase domain 30
CDHR1	-3.24111	0.000721	0.010362	-3.38165	Down	cadherin related family member 1
GJA10	-3.22733	0.000173	0.003765	-3.75491	Down	gap junction protein alpha 10
CYP3A43	-3.20066	3.99E-05	0.001294	-4.10804	Down	cytochrome P450 family 3 subfamily A member 43
BMP5	-3.18774	4.18E-06	0.000255	-4.60225	Down	bone morphogenetic protein 5
PRUNE2	-3.17519	1.38E-09	4.71E-07	-6.05767	Down	prune homolog 2 with BCH domain
LINC00602	-3.17107	0.000318	0.005801	-3.60012	Down	long intergenic non-protein coding RNA 602
RASD1	-3.16012	1.06E-09	3.74E-07	-6.10078	Down	ras related dexamethasone induced 1
TAAR9	-3.13989	0.003702	0.032231	-2.90248	Down	trace amine associated receptor 9
OR8H2	-3.12734	0.000427	0.007125	-3.5231	Down	olfactory receptor family 8 subfamily H member 2
INSRR	-3.11972	0.005572	0.042533	-2.77196	Down	insulin receptor related receptor
POSTN	-3.11052	1.26E-07	1.75E-05	-5.28454	Down	periostin
OR4N2	-3.09015	0.00604	0.044854	-2.74562	Down	olfactory receptor family 4 subfamily N member 2
CASQ2	-3.08655	0.001058	0.013583	-3.27466	Down	calsequestrin 2
LOC441204	-3.08411	7.24E-05	0.001987	-3.96836	Down	uncharacterized LOC441204
OR2A25	-3.08173	0.000264	0.005116	-3.64842	Down	olfactory receptor family 2 subfamily A member 25
OR5E1P	-3.0489	0.001755	0.019094	-3.12882	Down	olfactory receptor family 5 subfamily E member 1 pseudogene
LY6G6E	-3.04857	0.001493	0.017122	-3.17595	Down	lymphocyte antigen 6 family member G6E
SSTR5-AS1	-3.0425	8.27E-07	7.44E-05	-4.92887	Down	SSTR5 antisense RNA 1
CYP24A1	-3.03607	0.002253	0.022897	-3.0547	Down	cytochrome P450 family 24 subfamily A member 1
TAS2R7	-3.02863	0.000145	0.003362	-3.79889	Down	taste 2 receptor member 7

SLC8A1-AS1	-3.02422	0.000815	0.011262	-3.34768	Down	SLC8A1 antisense RNA 1
ZNF385D	-3.02118	7.51E-07	6.88E-05	-4.94777	Down	zinc finger protein 385D
LINC00460	-3.01407	0.001244	0.015147	-3.22856	Down	long intergenic non-protein coding RNA 460
KIF20A	-3.01006	0.000681	0.009971	-3.39723	Down	kinesin family member 20A
HLA-DQA1	-3.00395	1.85E-08	3.64E-06	-5.6257	Down	major histocompatibility complex, class II, DQ alpha 1
ASB5	-3.00067	0.000216	0.004436	-3.69951	Down	ankyrin repeat and SOCS box containing 5
OR1E2	-2.99957	0.001083	0.013816	-3.26804	Down	olfactory receptor family 1 subfamily E member 2
TNFAIP8	-2.99257	8.45E-15	1.70E-11	-7.7607	Down	TNF alpha induced protein 8
OR2B3	-2.98546	0.000293	0.005479	-3.62108	Down	olfactory receptor family 2 subfamily B member 3
SLC45A3	-2.97833	4.34E-05	0.001375	-4.08865	Down	solute carrier family 45 member 3
IFNA10	-2.97627	0.000425	0.007112	-3.52402	Down	interferon alpha 10
VWA5B1	-2.95932	0.001384	0.016227	-3.19796	Down	von Willebrand factor A domain containing 5B1
USP26	-2.95706	0.002713	0.026028	-2.99855	Down	ubiquitin specific peptidase 26
TM6SF2	-2.95528	2.99E-08	5.40E-06	-5.54201	Down	transmembrane 6 superfamily member 2
PPM1E	-2.94698	8.01E-06	0.000417	-4.46499	Down	protein phosphatase, Mg2+/Mn2+ dependent 1E
FOXM1	-2.94119	0.003185	0.029075	-2.94926	Down	forkhead box M1
TPX2	-2.93595	0.000949	0.012618	-3.30526	Down	TPX2 microtubule nucleation factor
LRRC10	-2.93393	0.002164	0.022223	-3.06669	Down	leucine rich repeat containing 10
GREM2	-2.92963	0.002908	0.027299	-2.97732	Down	gremlin 2, DAN family BMP antagonist
OR6N1	-2.92321	0.00263	0.025499	-3.00796	Down	olfactory receptor family 6 subfamily N member 1
EIF3IP1	-2.92189	0.003394	0.030322	-2.92956	Down	eukaryotic translation initiation factor 3 subunit I pseudogene 1
CAPN8	-2.91404	0.000476	0.007661	-3.49417	Down	calpain 8
GOLGA8CP	-2.90644	0.006607	0.047649	-2.71601	Down	golgin A8 family member C, pseudogene
TFF3	-2.89791	8.85E-06	0.000445	-4.44363	Down	trefoil factor 3
OR4K5	-2.89759	0.000785	0.011002	-3.35799	Down	olfactory receptor family 4 subfamily K member 5
HOPX	-2.89043	5.18E-06	0.000306	-4.55731	Down	HOP homeobox
MTRNR2L5	-2.88837	0.000627	0.009365	-3.41948	Down	MT-RNR2 like 5
COMP	-2.88387	9.00E-07	7.98E-05	-4.9123	Down	cartilage oligomeric matrix protein
OR4A5	-2.88266	0.000521	0.008166	-3.46976	Down	olfactory receptor family 4 subfamily A member 5
SULT1C2P1	-2.87268	0.000168	0.003688	-3.76253	Down	sulfotransferase family 1C member 2 pseudogene 1
OR5AN1	-2.86497	0.005374	0.041436	-2.78374	Down	olfactory receptor family 5 subfamily AN member 1
KRTAP1-3	-2.86473	0.002933	0.027411	-2.97471	Down	keratin associated protein 1-3
OR5AS1	-2.8631	0.00075	0.010703	-3.37055	Down	olfactory receptor family 5 subfamily AS member 1
GABRR2	-2.85852	0.001493	0.017122	-3.17608	Down	gamma-aminobutyric acid type A receptor subunit rho2
OR13G1	-2.85436	0.005275	0.040973	-2.78976	Down	olfactory receptor family 13 subfamily G member 1
OR2M5	-2.8505	0.001514	0.017284	-3.17193	Down	olfactory receptor family 2 subfamily M member 5
HTR3A	-2.82474	0.000642	0.009519	-3.41324	Down	5-hydroxytryptamine receptor 3A
KRTAP13-3	-2.82267	0.002954	0.027543	-2.97253	Down	keratin associated protein 13-3
OR13C5	-2.82057	7.98E-05	0.00213	-3.9449	Down	olfactory receptor family 13 subfamily C member 5
OR4C3	-2.80788	0.005491	0.042035	-2.77675	Down	olfactory receptor family 4 subfamily C member 3
PPIEL	-2.78532	4.64E-05	0.001444	-4.07319	Down	peptidylprolylisomerase E like pseudogene
ASB11	-2.78468	0.000245	0.004837	-3.66753	Down	ankyrin repeat and SOCS box containing 11
CHST8	-2.78461	1.89E-05	0.00076	-4.27789	Down	carbohydrate sulfotransferase 8

GOLGA6L1	-2.7816	0.000171	0.003726	-3.75848	Down	golgin A6 family like 1
MAS1	-2.77551	0.00044	0.007269	-3.51512	Down	MAS1 proto-oncogene, G protein-coupled receptor
OR52L1	-2.76744	8.16E-05	0.002168	-3.93961	Down	olfactory receptor family 52 subfamily L member 1
PBK	-2.76743	0.000196	0.004138	-3.72403	Down	PDZ binding kinase
ANXA2P3	-2.76623	0.001772	0.019268	-3.12596	Down	annexin A2 pseudogene 3
KRTAP4-2	-2.7586	0.001037	0.013422	-3.28017	Down	keratin associated protein 4-2
OR8K1	-2.75811	0.002112	0.021778	-3.07408	Down	olfactory receptor family 8 subfamily K member 1
TCN1	-2.75785	0.002731	0.026128	-2.99649	Down	transcobalamin 1
KIRREL3	-2.75601	0.000505	0.007982	-3.47799	Down	kirre like nephrin family adhesion molecule 3
OR6B2	-2.7546	0.003595	0.031565	-2.91164	Down	olfactory receptor family 6 subfamily B member 2
KRTAP19-1	-2.738	0.000419	0.007044	-3.52758	Down	keratin associated protein 19-1
KRTAP3-1	-2.73476	0.006721	0.048118	-2.71035	Down	keratin associated protein 3-1
SLCO5A1	-2.7339	0.000151	0.003436	-3.78966	Down	solute carrier organic anion transporter family member 5A1
IFNA1	-2.71621	0.003812	0.032859	-2.89328	Down	interferon alpha 1
KRTAP3-2	-2.71406	0.003974	0.033866	-2.8802	Down	keratin associated protein 3-2
VENTXP7	-2.70781	0.000793	0.011058	-3.35508	Down	VENT homeoboxpseudogene 7
LOC341056	-2.70401	0.004623	0.037645	-2.83218	Down	SUMO1 activating enzyme subunit 1 pseudogene
KRTAP9-9	-2.69101	0.005252	0.040848	-2.79118	Down	keratin associated protein 9-9
OR56A4	-2.68936	0.002123	0.021887	-3.07243	Down	olfactory receptor family 56 subfamily A member 4
FAM111B	-2.68489	0.000288	0.005416	-3.62612	Down	family with sequence similarity 111 member B
PSMA6	-2.68174	3.99E-18	1.80E-14	-8.67908	Down	proteasome 20S subunit alpha 6
DLGAP5	-2.68048	0.001477	0.017037	-3.17907	Down	DLG associated protein 5
PFKFB2	-2.67874	2.19E-10	9.91E-08	-6.34724	Down	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2
OR5B17	-2.67817	0.00413	0.034912	-2.86807	Down	olfactory receptor family 5 subfamily B member 17
LOC100287036	-2.66753	0.003578	0.031512	-2.91317	Down	uncharacterized LOC100287036
PCDH7	-2.66116	6.16E-07	6.09E-05	-4.98602	Down	protocadherin 7
MND1	-2.65071	2.22E-08	4.27E-06	-5.59402	Down	meiotic nuclear divisions 1
RCAN2	-2.60302	0.001595	0.01787	-3.15677	Down	regulator of calcineurin 2
TMEM108	-2.59295	5.48E-05	0.001641	-4.03417	Down	transmembrane protein 108
OR51A2	-2.58736	0.004723	0.038181	-2.82532	Down	olfactory receptor family 51 subfamily A member 2
P2RX5	-2.58657	0.000125	0.003005	-3.8356	Down	purinergic receptor P2X 5
SLC22A9	-2.58464	0.00124	0.01511	-3.22949	Down	solute carrier family 22 member 9
OR5T1	-2.57736	0.003632	0.031742	-2.90848	Down	olfactory receptor family 5 subfamily T member 1
OR1A1	-2.57723	0.002728	0.026111	-2.99685	Down	olfactory receptor family 1 subfamily A member 1
OR13C8	-2.57325	0.001945	0.020542	-3.09849	Down	olfactory receptor family 13 subfamily C member 8
OR13C2	-2.57298	0.005077	0.040061	-2.80213	Down	olfactory receptor family 13 subfamily C member 2
GAP43	-2.57224	0.001777	0.019296	-3.12518	Down	growth associated protein 43
MFAP5	-2.56407	0.000759	0.010785	-3.36736	Down	microfibril associated protein 5
SGPP2	-2.55582	2.11E-05	0.00082	-4.25256	Down	sphingosine-1-phosphate phosphatase 2
ADAMTSL1	-2.55426	1.36E-07	1.87E-05	-5.27081	Down	ADAMTS like 1
OR2L1P	-2.55171	0.000488	0.007806	-3.48701	Down	olfactory receptor family 2 subfamily L member 1 pseudogene
TPD52L3	-2.55159	0.001889	0.020166	-3.10709	Down	TPD52 like 3
PABPC1L2A	-2.55147	0.006252	0.045885	-2.73428	Down	poly(A) binding protein cytoplasmic 1 like 2A

OR51B4	-2.54936	0.001501	0.017188	-3.17446	Down	olfactory receptor family 51 subfamily B member 4
LCE1F	-2.54374	0.002888	0.027195	-2.97945	Down	late cornified envelope 1F
KCNQ2	-2.52303	0.001454	0.016864	-3.18366	Down	potassium voltage-gated channel subfamily Q member 2
SFRP4	-2.52066	1.03E-08	2.36E-06	-5.72526	Down	secreted frizzled related protein 4
KCNF1	-2.51814	0.000113	0.002775	-3.86075	Down	potassium voltage-gated channel modifier subfamily F member 1
OR2AG2	-2.51736	0.004873	0.038957	-2.8153	Down	olfactory receptor family 2 subfamily AG member 2
CD1E	-2.51051	0.002538	0.024876	-3.01877	Down	CD1e molecule
OR2M7	-2.50383	0.004156	0.03502	-2.86606	Down	olfactory receptor family 2 subfamily M member 7
OR51L1	-2.49986	0.001702	0.018656	-3.13791	Down	olfactory receptor family 51 subfamily L member 1
LINC00477	-2.49804	0.004433	0.036513	-2.8456	Down	long intergenic non-protein coding RNA 477
OR5H1	-2.49529	0.0037	0.032227	-2.90267	Down	olfactory receptor family 5 subfamily H member 1
FAM83E	-2.49154	0.000801	0.01113	-3.35243	Down	family with sequence similarity 83 member E
CRLF1	-2.48748	1.68E-12	1.60E-09	-7.05875	Down	cytokine receptor like factor 1
STAG3	-2.48528	0.002489	0.024577	-3.0247	Down	stromal antigen 3
KRTAP21-2	-2.47732	0.001534	0.017433	-3.16815	Down	keratin associated protein 21-2
OR8G1	-2.4672	0.005221	0.04074	-2.79305	Down	olfactory receptor family 8 subfamily G member 1
OR6K6	-2.46634	0.006059	0.044944	-2.74455	Down	olfactory receptor family 6 subfamily K member 6
KRTAP19-2	-2.4657	0.003103	0.028539	-2.95735	Down	keratin associated protein 19-2
OR10Z1	-2.45396	0.003252	0.029509	-2.94285	Down	olfactory receptor family 10 subfamily Z member 1
KRTAP10-1	-2.45298	0.006735	0.048175	-2.70969	Down	keratin associated protein 10-1
DNAH11	-2.45203	0.000344	0.006141	-3.57944	Down	dynein axonemal heavy chain 11
NPTX2	-2.44884	1.08E-10	5.76E-08	-6.455	Down	neuronal pentraxin 2
KCNH1	-2.44466	0.001977	0.020792	-3.0937	Down	potassium voltage-gated channel subfamily H member 1
OR4K1	-2.43709	0.004239	0.035455	-2.85982	Down	olfactory receptor family 4 subfamily K member 1
OR5T2	-2.43076	0.002914	0.027332	-2.97665	Down	olfactory receptor family 5 subfamily T member 2
PSMD6-AS2	-2.42892	0.000265	0.005132	-3.64722	Down	PSMD6 antisense RNA 2
EDARADD	-2.4128	9.72E-06	0.000474	-4.42333	Down	EDAR associated death domain
SDR16C5	-2.41156	0.00454	0.037128	-2.838	Down	short chain dehydrogenase/reductase family 16C member 5
LOC100130673	-2.41083	0.004883	0.03897	-2.81463	Down	phosphoribosyl pyrophosphate synthetase 2 pseudogene
PI16	-2.40562	0.000421	0.007072	-3.52631	Down	peptidase inhibitor 16
JPH2	-2.40312	0.00471	0.038127	-2.82621	Down	junctophilin 2
INSC	-2.40292	4.17E-06	0.000255	-4.60267	Down	INSC spindle orientation adaptor protein
FN1	-2.4003	9.15E-07	8.07E-05	-4.90913	Down	fibronectin 1
ACTBL2	-2.39082	0.003746	0.03246	-2.89875	Down	actin beta like 2
KIF4A	-2.37867	0.001252	0.015226	-3.22668	Down	kinesin family member 4A
VSIG10L	-2.37789	0.001623	0.018046	-3.15176	Down	V-set and immunoglobulin domain containing 10 like
GPD1	-2.37721	0.002655	0.025667	-3.00509	Down	glycerol-3-phosphate dehydrogenase 1
C1QL1	-2.37667	0.000214	0.004411	-3.7015	Down	complement C1q like 1
NPFF	-2.36906	8.90E-05	0.002312	-3.91888	Down	neuropeptide FF-amide peptide precursor
OR4N3P	-2.35827	0.005904	0.044102	-2.75305	Down	olfactory receptor family 4 subfamily N member 3 pseudogene
OR2A12	-2.34861	0.002721	0.026055	-2.99766	Down	olfactory receptor family 2 subfamily A member 12
CAPNS2	-2.34428	0.000221	0.004497	-3.69321	Down	calpain small subunit 2
OR5AK4P	-2.34022	0.006512	0.04726	-2.72083	Down	olfactory receptor family 5 subfamily AK member 4 pseudogene

BEND6	-2.33639	0.000272	0.005194	-3.64043	Down	BEN domain containing 6
YIPF4	-2.33303	6.30E-05	0.00178	-4.0014	Down	Yip1 domain family member 4
OR1L8	-2.33257	0.005375	0.041436	-2.78365	Down	olfactory receptor family 1 subfamily L member 8
FAM95B1	-2.31927	0.003903	0.033444	-2.88593	Down	family with sequence similarity 95 member B1
RDH16	-2.3132	0.00098	0.012875	-3.29622	Down	retinol dehydrogenase 16
HBD	-2.30048	0.006912	0.049	-2.70104	Down	hemoglobin subunit delta
OR1J2	-2.29925	0.005289	0.041019	-2.7889	Down	olfactory receptor family 1 subfamily J member 2
TAS2R60	-2.29771	0.000463	0.007527	-3.50125	Down	taste 2 receptor member 60
VSIG4	-2.29506	5.66E-07	5.69E-05	-5.00245	Down	V-set and immunoglobulin domain containing 4
IGF2BP3	-2.29121	0.000493	0.007844	-3.48429	Down	insulin like growth factor 2 mRNA binding protein 3
CHRNA10	-2.28988	0.003958	0.033807	-2.88147	Down	cholinergic receptor nicotinic alpha 10 subunit
OR5AP2	-2.25924	0.006852	0.048745	-2.70396	Down	olfactory receptor family 5 subfamily AP member 2
MEP1B	-2.25724	0.004207	0.035254	-2.86219	Down	meprin A subunit beta
UGT1A9	-2.25439	0.00578	0.043574	-2.76	Down	UDP glucuronosyltransferase family 1 member A9
OR52K1	-2.24884	0.004392	0.03629	-2.84857	Down	olfactory receptor family 52 subfamily K member 1
CYP26B1	-2.24879	0.000361	0.006326	-3.56691	Down	cytochrome P450 family 26 subfamily B member 1
FAT3	-2.24517	0.000527	0.008238	-3.46655	Down	FAT atypical cadherin 3
IL10	-2.24228	0.003217	0.029301	-2.94624	Down	interleukin 10
TNFRSF11A	-2.24044	7.07E-10	2.66E-07	-6.16461	Down	TNF receptor superfamily member 11a
GCGR	-2.23561	0.000942	0.012562	-3.30743	Down	glucagon receptor
RERGL	-2.21524	6.67E-06	0.000361	-4.50409	Down	RERG like
ZMAT4	-2.21188	0.004388	0.03629	-2.84882	Down	zinc finger matrin-type 4
CCDC54	-2.20591	0.004509	0.036964	-2.84014	Down	coiled-coil domain containing 54
OR9A2	-2.19677	0.006953	0.049212	-2.69909	Down	olfactory receptor family 9 subfamily A member 2
SPAG6	-2.19033	0.006245	0.045876	-2.73463	Down	sperm associated antigen 6
LOC401127	-2.18482	0.000134	0.003165	-3.81831	Down	WD repeat domain 5 pseudogene
ENTPD3	-2.18044	2.71E-12	2.23E-09	-6.99221	Down	ectonucleoside triphosphate diphosphohydrolase 3
LCN2	-2.16225	4.27E-05	0.001359	-4.09226	Down	lipocalin 2
TOP2A	-2.14257	0.001988	0.020883	-3.09206	Down	DNA topoisomerase II alpha
ACTL7A	-2.13887	0.002923	0.027371	-2.97574	Down	actin like 7A
OXGR1	-2.13657	0.003157	0.028911	-2.95204	Down	oxoglutarate receptor 1
MESP2	-2.13597	0.004817	0.038713	-2.81903	Down	mesoderm posterior bHLH transcription factor 2
CDH22	-2.13575	3.22E-05	0.001126	-4.15707	Down	cadherin 22
OR10A5	-2.13555	0.00036	0.006308	-3.56815	Down	olfactory receptor family 10 subfamily A member 5
SPC24	-2.13072	0.002388	0.023883	-3.03725	Down	SPC24 component of NDC80 kinetochore complex
LOC100506422	-2.12894	0.001293	0.015506	-3.21745	Down	putative deoxyuridine 5'-triphosphate nucleotidohydrolase-like protein FLJ16323
NSUN5P2	-2.12488	0.004023	0.034205	-2.87632	Down	NSUN5 pseudogene 2
KLHDC8A	-2.12063	0.001931	0.020472	-3.10071	Down	kelch domain containing 8A
ANKRD34C	-2.11947	0.005215	0.040726	-2.79342	Down	ankyrin repeat domain 34C
OR4C46	-2.11678	0.004308	0.035862	-2.85472	Down	olfactory receptor family 4 subfamily C member 46
LINC00671	-2.11267	0.000874	0.01186	-3.32835	Down	long intergenic non-protein coding RNA 671
UCHL1	-2.10092	0.000329	0.005946	-3.59133	Down	ubiquitin C-terminal hydrolase L1

HLA-C	-2.09812	0.001034	0.01341	-3.28109	Down	major histocompatibility complex, class I, C
CLEC4D	-2.09688	0.006021	0.044768	-2.74665	Down	C-type lectin domain family 4 member D
FGL1	-2.09534	2.36E-05	0.00089	-4.22771	Down	fibrinogen like 1
LRRC10B	-2.09389	0.001064	0.013642	-3.27304	Down	leucine rich repeat containing 10B
CDKN3	-2.09092	0.0001	0.002543	-3.88942	Down	cyclin dependent kinase inhibitor 3
TMEM200C	-2.08833	0.000653	0.009666	-3.40863	Down	transmembrane protein 200C
KANK4	-2.07825	0.000722	0.010375	-3.38106	Down	KN motif and ankyrin repeat domains 4
ACTC1	-2.07805	0.001404	0.016404	-3.1939	Down	actin alpha cardiac muscle 1
COL6A4P2	-2.06787	0.003406	0.030366	-2.92853	Down	collagen type VI alpha 4 pseudogene 2
VASP	-2.06614	9.06E-11	5.12E-08	-6.48188	Down	vasodilator stimulated phosphoprotein
LCN10	-2.05205	0.000462	0.00752	-3.50197	Down	lipocalin 10
MEG3	-2.04725	1.56E-08	3.21E-06	-5.65483	Down	maternally expressed 3
CIT	-2.04665	0.000351	0.00623	-3.57439	Down	citron rho-interacting serine/threonine kinase
CTNNA3	-2.03117	0.004056	0.034415	-2.87379	Down	catenin alpha 3
OR52W1	-2.02704	0.004903	0.039089	-2.81336	Down	olfactory receptor family 52 subfamily W member 1
IL5RA	-2.02549	0.006579	0.047591	-2.71742	Down	interleukin 5 receptor subunit alpha
RPL31	-2.02494	0.001538	0.017454	-3.16745	Down	ribosomal protein L31
CTSE	-2.00792	0.005802	0.043589	-2.75877	Down	cathepsin E
SOSTDC1	-2.00044	0.005797	0.043583	-2.75905	Down	sclerostin domain containing 1
TTC8	-1.99853	2.42E-07	2.95E-05	-5.16352	Down	tetratricopeptide repeat domain 8
RADIL	-1.98793	0.001675	0.018469	-3.14246	Down	Rap associating with DIL domain
TAS2R8	-1.98705	0.004385	0.03629	-2.84903	Down	taste 2 receptor member 8
OIP5	-1.97891	0.000709	0.010265	-3.38597	Down	Opa interacting protein 5
OLFM4	-1.97222	0.00062	0.009266	-3.42261	Down	olfactomedin 4
NDUFA8	-1.95217	1.65E-12	1.60E-09	-7.06142	Down	NADH:ubiquinoneoxidoreductase subunit A8
TSPAN1	-1.94046	1.70E-05	0.000707	-4.30155	Down	tetraspanin 1
SDHAP2	-1.93873	2.15E-07	2.68E-05	-5.18585	Down	succinate dehydrogenase complex flavoprotein subunit A pseudogene 2
MYCN	-1.92871	0.006923	0.049039	-2.70052	Down	MYCN proto-oncogene, bHLH transcription factor
GPR141	-1.91909	0.000936	0.012505	-3.30911	Down	G protein-coupled receptor 141
NTN1	-1.91802	6.50E-07	6.32E-05	-4.9757	Down	netrin 1
MAGEE2	-1.90962	0.000537	0.00834	-3.46166	Down	MAGE family member E2
EEF1A2	-1.90299	0.000516	0.008113	-3.47224	Down	eukaryotic translation elongation factor 1 alpha 2
MAP3K8	-1.90261	0.002553	0.024928	-3.01704	Down	mitogen-activated protein kinase kinasekinase 8
OR52E6	-1.89409	0.007	0.049484	-2.69686	Down	olfactory receptor family 52 subfamily E member 6
P2RX6	-1.8888	0.002619	0.025432	-3.00924	Down	purinergic receptor P2X 6
CTNNA2	-1.88542	0.001368	0.016106	-3.20124	Down	catenin alpha 2
SNORD17	-1.87942	0.000449	0.007397	-3.50975	Down	small nucleolar RNA, C/D box 17
DIRC3	-1.87831	0.00023	0.004625	-3.68404	Down	disrupted in renal carcinoma 3
KIF6	-1.87185	7.20E-06	0.000384	-4.4878	Down	kinesin family member 6
TTN	-1.86646	2.37E-05	0.00089	-4.22669	Down	titin
SAMD3	-1.85982	0.003005	0.027939	-2.96719	Down	sterile alpha motif domain containing 3
OR6K3	-1.85822	0.00637	0.046452	-2.72811	Down	olfactory receptor family 6 subfamily K member 3
QRICH2	-1.85193	7.62E-05	0.002061	-3.95612	Down	glutamine rich 2

RRM2	-1.85099	0.002235	0.022764	-3.05702	Down	ribonucleotidereductase regulatory subunit M2
BCO2	-1.84966	5.49E-05	0.001643	-4.03358	Down	beta-carotene oxygenase 2
MUSTN1	-1.84629	0.000187	0.003999	-3.73656	Down	musculoskeletal, embryonic nuclear protein 1
OR11H2	-1.84559	0.001589	0.017817	-3.1579	Down	olfactory receptor family 11 subfamily H member 2
ZNF695	-1.84353	0.000466	0.007558	-3.49967	Down	zinc finger protein 695
SULT1C2	-1.84327	0.000838	0.011496	-3.33987	Down	sulfotransferase family 1C member 2
GTF2H2C	-1.84144	2.42E-08	4.62E-06	-5.57866	Down	GTF2H2 family member C
TK1	-1.83218	0.000127	0.003035	-3.83165	Down	thymidine kinase 1
GINS2	-1.83103	6.19E-07	6.09E-05	-4.98512	Down	GINS complex subunit 2
CCR2	-1.82698	0.004504	0.036953	-2.84055	Down	C-C motif chemokine receptor 2
SHCBP1	-1.82541	0.005054	0.039942	-2.80359	Down	SHC binding and spindle associated 1
RAB11B-AS1	-1.8231	1.61E-05	0.000683	-4.31271	Down	RAB11B antisense RNA 1
PRAM1	-1.81806	0.005685	0.043083	-2.76544	Down	PML-RARA regulated adaptor molecule 1
NCKAP5	-1.81025	9.58E-07	8.38E-05	-4.90001	Down	NCK associated protein 5
P2RY12	-1.80448	1.20E-05	0.000557	-4.37801	Down	purinergic receptor P2Y12
CNN1	-1.80432	0.000511	0.008054	-3.47488	Down	calponin 1
HRC	-1.80167	5.89E-05	0.001709	-4.01703	Down	histidine rich calcium binding protein
CYP4Z1	-1.78642	0.005884	0.044023	-2.75418	Down	cytochrome P450 family 4 subfamily Z member 1
IP6K3	-1.78353	0.00152	0.017335	-3.17089	Down	inositol hexakisphosphate kinase 3
PTGS2	-1.7827	0.003252	0.029509	-2.94289	Down	prostaglandin-endoperoxide synthase 2
DEF8	-1.77864	0.000794	0.011065	-3.35471	Down	differentially expressed in FDCP 8 homolog
FOXD2	-1.77487	0.000539	0.008367	-3.46036	Down	forkhead box D2
APOC1	-1.77454	4.60E-05	0.001437	-4.07517	Down	apolipoprotein C1
LYZ	-1.77313	5.00E-05	0.001534	-4.0555	Down	lysozyme
ITGBL1	-1.76632	1.37E-07	1.87E-05	-5.26957	Down	integrin subunit beta like 1
GLP1R	-1.7604	9.18E-08	1.36E-05	-5.34227	Down	glucagon like peptide 1 receptor
CYP3A5	-1.75739	0.000151	0.003436	-3.79001	Down	cytochrome P450 family 3 subfamily A member 5
SH3BP2	-1.75378	0.00039	0.006665	-3.54652	Down	SH3 domain binding protein 2
SNORA47	-1.75268	8.24E-07	7.44E-05	-4.9295	Down	small nucleolar RNA, H/ACA box 47
NDRG4	-1.74784	0.002093	0.02164	-3.07666	Down	NDRG family member 4
KLRK1	-1.74544	0.000776	0.010938	-3.36131	Down	killer cell lectin like receptor K1
CNGA4	-1.73089	0.00257	0.025014	-3.01493	Down	cyclic nucleotide gated channel subunit alpha 4
APOC2	-1.71885	0.000977	0.012856	-3.29702	Down	apolipoprotein C2
SCD5	-1.71546	1.24E-07	1.74E-05	-5.28776	Down	stearoyl-CoA desaturase 5
KRTAP5-1	-1.71212	0.001104	0.014013	-3.26265	Down	keratin associated protein 5-1
FAM223A	-1.71176	0.006595	0.047609	-2.71663	Down	family with sequence similarity 223 member A
ANKRD23	-1.70813	1.69E-06	0.000135	-4.78678	Down	ankyrin repeat domain 23
HADH	-1.70627	3.96E-09	1.04E-06	-5.88592	Down	hydroxyacyl-CoA dehydrogenase
SERPINA3	-1.70483	0.00017	0.003704	-3.76058	Down	serpin family A member 3
OR52D1	-1.7042	0.004591	0.037466	-2.83438	Down	olfactory receptor family 52 subfamily D member 1
TMEM178A	-1.70223	0.002146	0.022047	-3.06927	Down	transmembrane protein 178A
BMS1P4	-1.69662	4.36E-07	4.67E-05	-5.05261	Down	BMS1 pseudogene 4
SMAD9	-1.68648	0.006737	0.048175	-2.70957	Down	SMAD family member 9

PIGP	-1.68357	4.36E-08	7.24E-06	-5.47564	Down	phosphatidylinositol glycan anchor biosynthesis class P
GALK2	-1.68337	2.87E-13	4.33E-10	-7.30016	Down	galactokinase 2
SNORA70E	-1.68291	0.001609	0.017966	-3.1543	Down	small nucleolar RNA, H/ACA box 70E
NEFM	-1.6821	4.63E-05	0.001444	-4.07361	Down	neurofilament medium
ZNF622	-1.67707	3.95E-08	6.81E-06	-5.49285	Down	zinc finger protein 622
EFNA4	-1.67629	0.001144	0.014391	-3.25251	Down	ephrin A4
LRP5L	-1.67397	1.35E-05	0.000604	-4.35245	Down	LDL receptor related protein 5 like
MED10	-1.67292	3.27E-06	0.000215	-4.65306	Down	mediator complex subunit 10
PIR	-1.67257	1.57E-07	2.11E-05	-5.24394	Down	pirin
HSD17B3	-1.67244	0.00193	0.020472	-3.10075	Down	hydroxysteroid 17-beta dehydrogenase 3
MRO	-1.66683	2.46E-05	0.000915	-4.21819	Down	maestro
PTGFR	-1.66615	4.11E-08	6.95E-06	-5.48615	Down	prostaglandin F receptor
GUSBP11	-1.66179	9.52E-08	1.40E-05	-5.33562	Down	GUSB pseudogene 11
CDK15	-1.66068	0.000948	0.012618	-3.30537	Down	cyclin dependent kinase 15
WDR3	-1.65943	1.43E-08	3.05E-06	-5.66959	Down	WD repeat domain 3
SCRG1	-1.65505	0.001442	0.016755	-3.1861	Down	stimulator of chondrogenesis 1
NR6A1	-1.65044	0.00046	0.007518	-3.50276	Down	nuclear receptor subfamily 6 group A member 1
FAM72D	-1.63864	0.00183	0.019741	-3.11653	Down	family with sequence similarity 72 member D
ZNF391	-1.63472	8.82E-06	0.000445	-4.44436	Down	zinc finger protein 391
CFB	-1.63155	0.000144	0.003338	-3.80159	Down	complement factor B
LGI2	-1.62508	2.48E-06	0.000175	-4.70977	Down	leucine rich repeat LGI family member 2
FCHO1	-1.62484	0.005264	0.04091	-2.79039	Down	FCH and mu domain containing endocytic adaptor 1
LRRC7	-1.62384	0.002558	0.024957	-3.01644	Down	leucine rich repeat containing 7
NEK6	-1.62009	0.00659	0.047609	-2.71687	Down	NIMA related kinase 6
LOC648987	-1.61592	0.003007	0.02794	-2.96703	Down	uncharacterized LOC648987
MMP28	-1.60978	0.000384	0.006598	-3.55064	Down	matrix metallopeptidase 28
LHFPL3-AS2	-1.60714	0.000745	0.010639	-3.37256	Down	LHFPL3 antisense RNA 2
AKR1C2	-1.60408	2.37E-05	0.00089	-4.22683	Down	aldo-ketoreductase family 1 member C2
BUB1B	-1.60351	0.005799	0.043583	-2.75895	Down	BUB1 mitotic checkpoint serine/threonine kinase B
LOC100507547	-1.60229	0.000828	0.011404	-3.34317	Down	uncharacterized LOC100507547
CDH23	-1.59792	0.001165	0.01459	-3.24742	Down	cadherin related 23
ANXA10	-1.59619	7.10E-06	0.000381	-4.49071	Down	annexin A10
ADAMTS2	-1.59391	7.57E-07	6.88E-05	-4.94615	Down	ADAM metallopeptidase with thrombospondin type 1 motif 2
PAPOLB	-1.58767	0.005074	0.040061	-2.80231	Down	poly(A) polymerase beta
CDKN1C	-1.58201	2.08E-06	0.000154	-4.74542	Down	cyclin dependent kinase inhibitor 1C
ATP2C1	-1.58082	0.001222	0.015003	-3.23363	Down	ATPase secretory pathway Ca2+ transporting 1
SPAG17	-1.57901	0.003276	0.029678	-2.94057	Down	sperm associated antigen 17
P2RY1	-1.57648	0.000798	0.011091	-3.35364	Down	purinergic receptor P2Y1
IGSF11	-1.57462	1.96E-05	0.000779	-4.26992	Down	immunoglobulin superfamily member 11
COMMD7	-1.57449	0.000354	0.006238	-3.57221	Down	COMM domain containing 7
LOC440173	-1.5733	0.000203	0.004248	-3.71519	Down	uncharacterized LOC440173
UBXN10	-1.56955	0.003965	0.033807	-2.8809	Down	UBX domain protein 10
TSHZ3	-1.56942	3.81E-05	0.001252	-4.11863	Down	teashirt zinc finger homeobox 3

LRRC39	-1.56781	0.00276	0.02628	-2.99327	Down	leucine rich repeat containing 39
PDLIM3	-1.56765	3.35E-05	0.001154	-4.14833	Down	PDZ and LIM domain 3
IFI27L2	-1.56751	0.004728	0.038202	-2.825	Down	interferon alpha inducible protein 27 like 2
EFCAB12	-1.56177	0.005243	0.040847	-2.79172	Down	EF-hand calcium binding domain 12
SCGB2A1	-1.56061	0.005011	0.039689	-2.80634	Down	secretoglobin family 2A member 1
CRYGS	-1.56043	0.003935	0.033661	-2.88331	Down	crystallin gamma S
ARHGAP20	-1.55688	0.001308	0.015618	-3.21424	Down	Rho GTPase activating protein 20
FRMPD1	-1.54919	0.001419	0.016541	-3.19075	Down	FERM and PDZ domain containing 1
KIF20B	-1.54488	0.001915	0.020374	-3.10318	Down	kinesin family member 20B
SELL	-1.54158	0.003719	0.032311	-2.90103	Down	selectin L
NEDD8	-1.54099	4.08E-09	1.04E-06	-5.88096	Down	NEDD8 ubiquitin like modifier
RASSF1	-1.54021	0.000352	0.006238	-3.57352	Down	Ras association domain family member 1
ESR1	-1.53465	0.003504	0.030999	-2.91966	Down	estrogen receptor 1
ERVK13-1	-1.52459	0.000155	0.003502	-3.78254	Down	endogenous retrovirus group K13 member 1
HEBP2	-1.51608	1.06E-06	9.13E-05	-4.88012	Down	heme binding protein 2
ARHGAP22	-1.51421	0.002497	0.024632	-3.02369	Down	Rho GTPase activating protein 22
TYW1B	-1.51088	2.73E-06	0.000187	-4.69036	Down	tRNA-yW synthesizing protein 1 homolog B
AGAP2	-1.51064	0.003808	0.03285	-2.89366	Down	ArfGAP with GTPase domain, ankyrin repeat and PH domain 2
CYP4F12	-1.5094	0.004865	0.038909	-2.81584	Down	cytochrome P450 family 4 subfamily F member 12
RASD2	-1.50824	1.28E-06	0.000107	-4.84244	Down	RASD family member 2
SLC26A7	-1.50389	0.002177	0.022312	-3.06497	Down	solute carrier family 26 member 7
LY6G5B	-1.49949	0.002268	0.023028	-3.05265	Down	lymphocyte antigen 6 family member G5B
TFCP2L1	-1.49843	5.31E-06	0.000312	-4.55219	Down	transcription factor CP2 like 1
CSF2RA	-1.49594	0.002137	0.02198	-3.07048	Down	colony stimulating factor 2 receptor subunit alpha
TDH	-1.49341	0.001129	0.014269	-3.25632	Down	L-threonine dehydrogenase (pseudogene)
RELT	-1.49125	0.001848	0.019864	-3.11363	Down	RELT TNF receptor
MAP1A	-1.48562	0.001649	0.018241	-3.14714	Down	microtubule associated protein 1A
LOXL1	-1.48506	0.000251	0.004917	-3.66139	Down	lysyl oxidase like 1
KIF18A	-1.48239	0.001571	0.017708	-3.16123	Down	kinesin family member 18A
B3GNT3	-1.47982	0.002083	0.021574	-3.07809	Down	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 3
LOC646214	-1.47392	0.001568	0.017688	-3.16181	Down	p21 (RAC1) activated kinase 2 pseudogene
PRICKLE4	-1.47244	0.003718	0.032311	-2.90114	Down	prickle planar cell polarity protein 4
MYO1F	-1.47133	0.000544	0.008416	-3.45796	Down	myosin IF
JMJD6	-1.47043	4.70E-07	4.99E-05	-5.03799	Down	jumonji domain containing 6, arginine demethylase and lysine hydroxylase
TXNDC9	-1.46925	6.09E-13	7.86E-10	-7.19855	Down	thioredoxin domain containing 9
STXBP5-AS1	-1.4673	0.002667	0.025755	-3.00372	Down	STXBP5 antisense RNA 1
LUC7L	-1.46492	1.72E-06	0.000136	-4.78434	Down	LUC7 like
ARG2	-1.46353	0.002923	0.027371	-2.97571	Down	arginase 2
POU5F1	-1.45988	0.006916	0.049011	-2.70084	Down	POU class 5 homeobox 1
ARHGAP9	-1.45129	0.002566	0.025001	-3.01541	Down	Rho GTPase activating protein 9
LINC00239	-1.45125	0.001024	0.013326	-3.28388	Down	long intergenic non-protein coding RNA 239
MS4A7	-1.44992	2.59E-05	0.000948	-4.20697	Down	membrane spanning 4-domains A7
ROBO1	-1.44661	0.000429	0.007144	-3.52164	Down	roundabout guidance receptor 1

TRIM66	-1.44341	5.54E-06	0.000322	-4.5431	Down	tripartite motif containing 66
ALOX5	-1.43679	1.24E-07	1.74E-05	-5.28802	Down	arachidonate 5-lipoxygenase
GPX2	-1.43654	0.000227	0.004581	-3.68729	Down	glutathione peroxidase 2
EXOSC8	-1.43535	3.46E-10	1.40E-07	-6.27648	Down	exosome component 8
NUSAP1	-1.43456	0.001488	0.017083	-3.17698	Down	nucleolar and spindle associated protein 1
ANLN	-1.43239	0.004239	0.035455	-2.8598	Down	anillin actin binding protein
CDK1	-1.43222	0.001258	0.015231	-3.22537	Down	cyclin dependent kinase 1
SELPLG	-1.43155	0.000579	0.008821	-3.44138	Down	selectin P ligand
GREB1	-1.42927	3.36E-07	3.75E-05	-5.10196	Down	growth regulating estrogen receptor binding 1
MYH11	-1.42608	0.004478	0.036813	-2.84233	Down	myosin heavy chain 11
ABCB1	-1.42508	0.001795	0.019432	-3.12223	Down	ATP binding cassette subfamily B member 1
CHCHD1	-1.41714	0.001135	0.014326	-3.25479	Down	coiled-coil-helix-coiled-coil-helix domain containing 1
PDE1C	-1.41678	0.001008	0.013153	-3.28817	Down	phosphodiesterase 1C
DLG2	-1.41507	6.13E-05	0.001753	-4.00758	Down	discs large MAGUK scaffold protein 2
SNORA57	-1.41264	0.000168	0.00368	-3.76338	Down	small nucleolar RNA, H/ACA box 57
COQ5	-1.41257	1.02E-06	8.87E-05	-4.88694	Down	coenzyme Q5, methyltransferase
CYP2J2	-1.40784	7.09E-05	0.001948	-3.97338	Down	cytochrome P450 family 2 subfamily J member 2
TEKT2	-1.40714	0.001087	0.013854	-3.26686	Down	tektin 2
CPA4	-1.39844	0.002227	0.022694	-3.05821	Down	carboxypeptidase A4
OR4F3	-1.39842	0.006622	0.04769	-2.71528	Down	olfactory receptor family 4 subfamily F member 3
ADAMTS10	-1.39793	0.00084	0.011516	-3.33917	Down	ADAM metallopeptidase with thrombospondin type 1 motif 10
VAV3	-1.39763	3.65E-06	0.000231	-4.63055	Down	vav guanine nucleotide exchange factor 3
HSD17B7P2	-1.39759	1.68E-05	0.000705	-4.30357	Down	hydroxysteroid 17-beta dehydrogenase 7 pseudogene 2
TYMS	-1.39182	8.67E-05	0.00227	-3.92507	Down	thymidylatesynthetase
SCN1B	-1.39167	3.70E-06	0.000233	-4.62739	Down	sodium voltage-gated channel beta subunit 1
LAT	-1.38953	0.001091	0.013873	-3.26588	Down	linker for activation of T cells
SNORA71B	-1.3858	0.001448	0.016813	-3.18491	Down	small nucleolar RNA, H/ACA box 71B
SMIM5	-1.38397	0.002396	0.023909	-3.03617	Down	small integral membrane protein 5
MATN3	-1.38264	0.00087	0.011855	-3.32948	Down	matrilin 3
RNASE2	-1.37954	0.004946	0.039334	-2.81051	Down	ribonuclease A family member 2
SWT1	-1.36623	1.40E-05	0.000618	-4.3442	Down	SWT1 RNA endoribonuclease homolog
LAMB3	-1.36487	0.002986	0.027804	-2.96915	Down	laminin subunit beta 3
LINC00244	-1.36128	0.005216	0.040726	-2.79338	Down	long intergenic non-protein coding RNA 244
PRODH	-1.36073	0.001733	0.018929	-3.1326	Down	proline dehydrogenase 1
SRD5A1	-1.35922	4.03E-06	0.000249	-4.60986	Down	steroid 5 alpha-reductase 1
SRPX2	-1.35844	5.74E-07	5.74E-05	-4.99961	Down	sushi repeat containing protein X-linked 2
APOBEC2	-1.35451	1.34E-06	0.000111	-4.8333	Down	apolipoprotein B mRNA editing enzyme catalytic subunit 2
PKDREJ	-1.35249	0.002568	0.025007	-3.01517	Down	polycystin family receptor for egg jelly
SGIP1	-1.35053	0.000715	0.010307	-3.38374	Down	SH3GL interacting endocytic adaptor 1
NAPSB	-1.34741	0.001225	0.015005	-3.23311	Down	napsin B aspartic peptidase, pseudogene
MBL1P	-1.34188	0.004945	0.039334	-2.81059	Down	mannose binding lectin 1, pseudogene
SLC7A7	-1.33735	1.58E-05	0.000674	-4.31659	Down	solute carrier family 7 member 7
GLG1	-1.33647	4.71E-07	4.99E-05	-5.03762	Down	golgi glycoprotein 1

SNORA10	-1.33039	0.001471	0.017006	-3.18032	Down	small nucleolar RNA, H/ACA box 10
TPM2	-1.32665	6.85E-08	1.04E-05	-5.39512	Down	tropomyosin 2
MEG8	-1.32203	1.68E-07	2.23E-05	-5.23175	Down	maternally expressed 8, small nucleolar RNA host gene
ASB16	-1.32095	5.04E-05	0.001536	-4.05368	Down	ankyrin repeat and SOCS box containing 16
RAD51AP1	-1.31844	0.001646	0.018238	-3.14755	Down	RAD51 associated protein 1
TBC1D3	-1.31758	0.000265	0.005132	-3.6469	Down	TBC1 domain family member 3
SIX2	-1.31048	0.000344	0.006141	-3.57942	Down	SIX homeobox 2
TBC1D3F	-1.30768	0.000476	0.007661	-3.49393	Down	TBC1 domain family member 3F
SAMHD1	-1.30624	3.02E-08	5.40E-06	-5.54048	Down	SAM and HD domain containing deoxynucleoside triphosphate triphosphohydrolase 1
FAM227A	-1.3019	0.001032	0.01339	-3.28173	Down	family with sequence similarity 227 member A
LOC100506123	-1.30135	0.001802	0.019495	-3.12109	Down	uncharacterized LOC100506123
SERTAD4-AS1	-1.30081	0.003311	0.029845	-2.93729	Down	SERTAD4 antisense RNA 1

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

GO ID	**CATEGORY**	**GO Name**	**Adjusted p value**	**negative log10 of adjusted p value**	**Gene Count**	**Gene**
			Up regulated genes			
GO:0007275	BP	multicellular organism development	1.03027E-05	4.987047489	192	IGF2,KRT6A,LCE3D,SPRR3,FLG,SPRR2D,SPRR1B,SLITRK6,FGF21,TBX22,CALCR,SPRR1A,USH2A,OTX2,DCC,KCP,NOG,STAR,KRT16,IL1RN,SHISA2,AQP5,SYNDIG1,TFAP2C,ERRFI1,PLP1,ALOX12,KRT13,SPRR2E,TENM1,PEMT,LY6H,FAP,EYA4,LCE3E,EGR1,CSGALNACT1,MAL,MMP16,PTGER4,COL6A3,OAS2,ETV4,MAOB,GPC6,SOCS5,BCL9,POU6F2,BTG2,PRR15,VEGFC,FAM20C,MPZ,TMEM176A,KLK13,RPS6,ID3,ALOXE3,DDIT4,IRF2BP2,KLF15,EGR3,RNF165,LTBP4,CREB3L1,EMX1,KLF3,ZFP36,QDPR,ETV5,KL,GADD45B,NXN,TLE3,HEYL,HRAS,GLI3,SFTPD,MYC,IGSF8,DMD,FKBP8,DBP,MTCH1,KLF10,PODXL,BVES,MNT,LSR,CEL,FOSL2,WASF1,PAPSS2,NR1D1,DUSP4,SNX19,FOXN3,IL6ST,IL6R,PCDHB6,KLF6,ZFP36L1,PBX1,SH3RF1,CNTN3,NHEJ1,BOC,STAT1,DUSP1,CLSTN2,DIP2B,MYADM,PCDHB11,APOD,NR0B2,NHS,SYVN1,TCF7L2,DLL4,NNMT,SMAD1,TP53,PCDH18,SUN2,SOS1,PRKACA,EGFR,ETS1,PIK3CA,TSHZ1,GCNT2,PKN1,TNFRSF1A,ELOVL1,NCS

						TN,MFAP2,YBX1,PLCE1,NDST1,KCNJ8,GAMT,DGCR2,TPI1,JMJD8,NES,WDTC1,MAML1,PCDHB4,NFIB,MAPK3,SLC23A2,FOXK1,CAMSAP3,ACVR2B,PLOD3,ZFHX3,SMURF1,PRMT6,PRKCSH,ETV6,GSK3A,WDR74,BCOR,NPAS2,USP1,RBM47,RNF43,TCOF1,NCL,METTL14,KCTD11,HSP90AA1,BTG1,GAB1,S1PR1,THRB,EDNRB,SYBU,CDNF,MEX3C,SIAH2,NFKBIA,GJA1,CD34,DEAF1,INSR,NR1D2,GADD45G,ZNRF3,MBOAT7,BSG,BTF3
GO:0006807	BP	nitrogen compound metabolic process	8.09009E-05	4.092046627	292	CRNN,PGA5,CGA,FGA,IGF2,FGB,APOA5,SPRR3,FLG,SPRR1B,FGF21,FGG,TBX22,CALCR,PGC,SPRR1A,ABCB11,OTX2,MUC21,NOG,HSFX2,ZSCAN10,TFAP2C,ERRFI1,RUNX1T1,ALOX12,SPRR2E,PDK4,TENM1,HAO1,PEMT,FAP,EYA4,ZNF554,EGR1,CSGALNACT1,GCG,MMP16,ADAMTS8,COL6A3,MAPK4,OAS2,ETV4,MAOB,GPC6,SOCS5,GMNC,BCL9,PDK3,POU6F2,BTG2,A4GNT,CST6,VEGFC,FAM20C,USP27X,STK32B,KLK13,RPS6,ID3,PGAP2,ALOXE3,LSM11,BCAP31,DDIT4,DPP4,TYSND1,IRF2BP2,KLF15,EGR3,RNF165,PHLDA1,LTBP4,IKZF4,CREB3L1,A1CF,EMX1,NAT10,ACSL6,KLF3,ZFP36,QDPR,OAS1,ETV5,GADD45B,MAN1A1,NXN,TLE3,RPL8,HEYL,PER3,HRAS,GLI3,SFTPD,MYC,RPRD2,DMD,ZNF416,FKBP8,RPS28,DBP,MUC6,MTCH1,CHST10,KLF9,EIF4B,KLF10,GLTP,MNT,CEL,NUP205,FOSL2,ZNF362,PAPSS2,NR1D1,DUSP4,SMCR8,FECH,FOXN3,IL6ST,IL6R,ZNF581,KLF6,CPA1,ABCA1,ZFP36L1,PBX1,SH3RF1,URM1,ERN1,RPL18,RNF24,PRRC1,NHEJ1,PDK2,STAT1,HSPA2,DUSP1,DIP2B,FMOD,MYADM,APOD,GLS,FBXO32,SRM,DIRAS3,NR0B2,SYVN1,ARL6IP1,TCF7L2,TMUB1,MRPL37,DLL4,HELZ2,NNMT,SMAD1,TP53,ELK1,PTBP1,PRKACA,BACH2,CTSF,EGFR,ETS1,PIK3CA,ZNRF1,CMPK2,GUK1,TSHZ1,ZNF326,MED13L,GCNT2,SAE1,PKN1,TNFRSF1A,ELOVL1,TUT1,NCSTN,YBX1,PPP1R3B,PLCE1,NDST1,ATF6B,GAMT,TPI1,JMJD8,SECISBP2L,

						PRPF8,EIF3B,WDTC1,MAML1,CRNKL1,NFIB,MAPK3,RPL18A,CNDP2,SERTAD2,RCE1,FOXK1,ZNF646,ACVR2B,PLOD3,ZFHX3,SMURF1,AOX1,RPS15,PRMT6,TRIM24,PRKCSH,ETV6,GSK3A,WDR74,LARP6,BCOR,URB1,ZNF341,SGTA,STUB1,NPAS2,MAOA,USP1,RBM47,RNF43,SHISA5,TCOF1,NCL,FKBP5,RBM22,METTL14,PIGM,ATF7IP,POLR1D,UBAP2,UBE2E2,SPPL3,KCTD11,HSP90AA1,BTG1,S1PR1,THRB,RPL39,UTP14A,EDNRB,CRTC3,AK1,MED25,ERP29,RBM23,RNASEK,LPCAT3,CASC3,MTMR3,TNKS,SF3A1,ADPRHL1,MEX3C,SIAH2,ACD,NFKBIA,GJA1,RNPS1,ATP13A2,TXNDC5,MRPL49,SLC35C2,CD34,SQSTM1,DEAF1,INSR,RPL19,NR1D2,AGBL5,SP2,SLC2A4RG,MRPS18B,NEDD9,GADD45G,ZNRF3,MAST3,SNX12,BAZ2A,MBOAT7,GID8,DCPS,LIG3,SP4,KLF11,CIZ1,LNX1,RALB,BTF3,ZNF836
GO:0031974	CC	membrane-enclosed lumen	0.000311835	3.506075034	175	PGA5,CGA,FGA,IGF2,FGB,APOA5,FGG,MUC21,STAR,ZSCAN10,TFAP2C,RUNX1T1,SLC7A14,PDK4,TENM1,HAO1,ZNF554,EGR1,GCG,MMP16,COL6A3,MAPK4,OAS2,ETV4,GPC6,BCL9,PDK3,VEGFC,FAM20C,RPS6,LSM11,TYSND1,IRF2BP2,KLF15,PHLDA1,IKZF4,A1CF,EMX1,NAT10,KLF3,OAS1,ETV5,GRIK5,GPR63,TLE3,HEYL,HRAS,GLI3,MYC,RPRD2,IRS1,RPS28,MUC6,KLF9,PODXL,MNT,NUP205,FOSL2,NR1D1,DUSP4,SMCR8,FECH,KLF6,PBX1,RPL18,ABCG2,NHEJ1,PDK2,SELENBP1,STAT1,HSPA2,FMOD,GLS,FBXO32,NR0B2,NHS,SYVN1,TCF7L2,TMUB1,MRPL37,HELZ2,SMAD1,TP53,ELK1,SUN2,PTBP1,PRKACA,BACH2,TOR2A,CTSF,EGFR,ETS1,CMPK2,C17ORF49,ZNF326,SAE1,PKN1,TUT1,YBX1,ME2,JMJD8,PRPF8,WDTC1,MAML1,CRNKL1,NFIB,MAPK3,CNDP2,SERTAD2,FOXK1,CAMSAP3,PLOD3,FAM193B,ZFHX3,SMURF1,RPS15,PRMT6,TRIM24,PRKCSH,ETV6,WDR74,BCOR,URB1,STUB1,NPAS2,USP1,SHISA5,TCOF1,NCL,FKBP5,RBM22,METTL14,MZT2B,ATF7IP,POLR

						1D,FIGN,HSP90AA1,BTG1,S1PR1,THRB,UTP14A,CRTC3,MED25,ERP29,CASC3,TNKS,SF3A1,CHID1,SIAH2,ACD,NFKBIA,ARHGAP17,GJA1,RNPS1,ATP13A2,TXNDC5,MRPL49,SLC35C2,SQSTM1,DEAF1,INSR,RPL19,NR1D2,SP2,SLC2A4RG,MRPS18B,NEDD9,BAZ2A,CCDC86,GID8,DCPS,LIG3,SP4,KLF11,CIZ1
GO:0031981	CC	nuclear lumen	0.004404749	2.356078816	139	ZSCAN10,TFAP2C,RUNX1T1,SLC7A14,TENM1,ZNF554,EGR1,MAPK4,OAS2,ETV4,BCL9,PDK3,RPS6,LSM11,IRF2BP2,KLF15,PHLDA1,IKZF4,A1CF,EMX1,NAT10,KLF3,OAS1,ETV5,GRIK5,GPR63,TLE3,HEYL,HRAS,GLI3,MYC,RPRD2,IRS1,RPS28,KLF9,PODXL,MNT,NUP205,FOSL2,NR1D1,DUSP4,SMCR8,KLF6,PBX1,RPL18,ABCG2,NHEJ1,PDK2,SELENBP1,STAT1,HSPA2,FBXO32,NR0B2,NHS,SYVN1,TCF7L2,TMUB1,HELZ2,SMAD1,TP53,ELK1,SUN2,PTBP1,PRKACA,BACH2,ETS1,CMPK2,C17ORF49,ZNF326,SAE1,PKN1,TUT1,YBX1,PRPF8,WDTC1,MAML1,CRNKL1,NFIB,MAPK3,CNDP2,SERTAD2,FOXK1,CAMSAP3,FAM193B,ZFHX3,SMURF1,RPS15,PRMT6,TRIM24,ETV6,WDR74,BCOR,URB1,STUB1,NPAS2,USP1,TCOF1,NCL,FKBP5,RBM22,METTL14,MZT2B,ATF7IP,POLR1D,FIGN,HSP90AA1,BTG1,S1PR1,THRB,UTP14A,CRTC3,MED25,CASC3,TNKS,SF3A1,SIAH2,ACD,NFKBIA,ARHGAP17,GJA1,RNPS1,SLC35C2,SQSTM1,DEAF1,INSR,RPL19,NR1D2,SP2,SLC2A4RG,MRPS18B,NEDD9,BAZ2A,CCDC86,GID8,DCPS,LIG3,SP4,KLF11,CIZ1
GO:0005515	MF	protein binding	0.010406822	1.982681882	384	CRNN,CGA,FGA,IGF2,KRT6A,FGB,LCE3D,SLC6A15,APOA5,SPRR3,FLG,SLITRK6,FGF21,FGG,TBX22,CALCR,SPRR1A,ABCB11,USH2A,OTX2,HBM,DCC,POTED,KCP,RGPD3,NOG,STAR,KRT16,HSFX2,IL1RN,ZSCAN10,SHISA2,TACR1,AQP5,SYNDIG1,TFAP2C,ERRFI1,TMEM174,CNTNAP4,PLP1,RUNX1T1,ALOX12,KRT13,SLC7A14,SPRR2E,PDK4,TENM1,PRLHR,SLC22A11,PEMT,LY6H,TMEM236,FAP,EYA4,BTBD11,FBP2,LCE3E,ZNF554,EGR1,CSGALNACT1,MT2A

,MAL,SLC38A4,GCG,ASIC1,ADAMTS8,PTGER4,TMEM201,COL6A3,MAPK4,OAS2,AQP7,SLC25A48,ETV4,MAOB,GPC6,KCNJ2,MT1E,SOCS5,GMNC,BCL9,PDK3,ABCC9,POU6F2,BTG2,CST6,PRR15,VEGFC,FAM20C,C16ORF89,TMEM176A,KLK13,RPS6,ID3,PGAP2,ALOXE3,LSM11,BCAP31,DDIT4,DPP4,TYSND1,KLF15,RNF165,AQP8,SLC22A17,PHLDA1,FAM86B2,LTBP4,IKZF4,CREB3L1,A1CF,EMX1,NAT10,NETO2,ACSL6,KLF3,ZFP36,QDPR,OAS1,ETV5,GRIK5,KL,ZNF385C,GADD45B,SLC29A3,CGREF1,TLE3,RPL8,HEYL,PER3,HRAS,GLI3,WDR89,KIAA0408,SFTPD,MYC,TTI1,IFIT3,IGSF8,RPRD2,DMD,AQP12B,FKBP8,IRS1,KIAA1958,RPS28,TMEM140,MUC6,MTCH1,ABHD15,EIF4B,KLF10,PODXL,BVES,GLTP,MNT,CEL,NUP205,FOSL2,SLC1A5,WASF1,PAPSS2,TMCO4,NR1D1,DUSP4,SNX19,SMCR8,FECH,FOXN3,IL6ST,IL6R,PCDHB6,ZNF581,KLF6,CPA1,ABCA1,ZFP36L1,PBX1,DYSF,SH3RF1,PLEKHG6,URM1,ERN1,RPL18,CNTN3,CYGB,RNF24,ABCG2,PRRC1,NHEJ1,PDK2,BOC,SELENBP1,STAT1,HSPA2,DUSP1,DIP2B,FMOD,MYADM,ARPC1A,KCTD12,APOD,GLS,FBXO32,SRM,DIRAS3,NR0B2,SYVN1,ARL6IP1,TCF7L2,TMUB1,DHRS11,DLL4,HELZ2,SMAD1,TP53,PCDH18,ELK1,SUN2,TMEM150A,PTBP1,SOS1,PRKACA,BACH2,TOR2A,EGFR,ETS1,PIK3CA,ZNRF1,C17ORF49,GUK1,ZNF326,GCNT2,SAE1,GTPBP8,PKN1,TNFRSF1A,ELOVL1,TUT1,NCSTN,MFAP2,YBX1,PPP1R3B,PLCE1,NDST1,KCNJ8,ATF6B,GAMT,DGCR2,TPI1,JMJD8,NES,CDC42EP3,SECISBP2L,PRPF8,DNAJC4,EIF3B,EPHX1,WDTC1,MAML1,CRNKL1,MAPK3,RPL18A,FAM83B,SERTAD2,FOXK1,ZNF646,CAMSAP3,ACVR2B,ATXN7L1,LRRC8B,PLOD3,FAM193B,ZFHX3,SMURF1,AOX1,RPS15,PRMT6,TRIM24,PRKCSH,ETV6,GSK3A,WDR74,KCNC4,LARP6,BCOR,PSD4,RAB4A,ZNF341,SGTA,STUB1,SLC35E1,NPAS2,MAOA,USP1,

						RBM47,RNF43,KIAA0930,SHISA5,TCOF1,NCL,FKBP5,RBM22,SLC48A1,TRAPPC3,METTL14,MZT2B,ATF7IP,RWDD2B,POLR1D,UBIAD1,SFXN2,FIGN,UBAP2,UBE2E2,MX1,SPPL3,KCTD11,HSP90AA1,BTG1,GAB1,PXMP2,S1PR1,THRB,UTP14A,EDNRB,CRTC3,SYBU,MED25,ERP29,RBM23,CDNF,RNASEK,CASC3,MTMR3,TNKS,SF3A1,CHID1,AGPAT3,MEX3C,SIAH2,ACD,NFKBIA,CDC42EP4,ARHGAP17,GJA1,RNPS1,ATP13A2,ZSWIM3,TXNDC5,PPFIBP2,MRPL49,SLC35C2,CD34,SQSTM1,DEAF1,CPNE8,INSR,RPL19,NR1D2,AGBL5,SP2,YIPF3,MRPS18B,NEDD9,GADD45G,ZNRF3,MAST3,SNX12,TMED5,BAZ2A,CCDC86,MBOAT7,GID8,DCPS,LIG3,BSG,SP4,KLF11,CIZ1,LNX1,RALB,BTF3,NET1
GO:0140110	MF	transcription regulator activity	0.019982707	1.699345683	71	TBX22,OTX2,HSFX2,ZSCAN10,TFAP2C,RUNX1T1,ZNF554,EGR1,ETV4,BCL9,POU6F2,BTG2,IRF2BP2,KLF15,EGR3,IKZF4,CREB3L1,EMX1,KLF3,ETV5,TLE3,HEYL,GLI3,MYC,ZNF416,DBP,KLF9,KLF10,MNT,FOSL2,ZNF362,NR1D1,FOXN3,ZNF581,KLF6,PBX1,STAT1,NR0B2,TCF7L2,HELZ2,SMAD1,TP53,ELK1,BACH2,ETS1,TSHZ1,MED13L,PKN1,ATF6B,MAML1,NFIB,SERTAD2,FOXK1,ZNF646,ZFHX3,TRIM24,ETV6,BCOR,ZNF341,NPAS2,ATF7IP,BTG1,THRB,SIAH2,DEAF1,NR1D2,SP2,SLC2A4RG,SP4,KLF11,ZNF836
Down regulated genes						
GO:0051606	BP	detection of stimulus	9.55E-21	20.01997014	63	DMBT1,OR10J3,OR4F5,OR6C74,OR5L1,OR4D2,OR2T33,OR2T6,GJA10,OR8H2,OR4N2,CASQ2,OR2A25,TAS2R7,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,OR13G1,OR2M5,OR13C5,OR4C3,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,OR2A12,OR1L8,OR1J2,TAS2R60,CHRNA10,OR5AP2,OR52K1,OR9A2,OR10A5,OR4C46,OR52W1,TAS2R8,OR52E6,TTN,OR6K3,OR11H2,OR52D1,PKDREJ
GO:0032501	BP	multicellular organismal process	3.26E-07	6.486491268	224	IAPP,HAPLN4,ADCYAP1,DMBT1,RGS16,PREX1,NR

G3,LRRTM3,GABRA2,GTSF1,NTNG2,GLRA1,DGKG,ISX,OR10J3,SLC6A17,DACH2,IFNA16,OR4F5,SLC18A2,KLHL1,OR6C74,DKK4,UNC5A,OR5L1,OR4D2,OR2T33,OR2T6,CDHR1,GJA10,BMP5,OR8H2,INSRR,POSTN,OR4N2,CASQ2,OR2A25,CYP24A1,TAS2R7,OR1E2,OR2B3,SLC45A3,IFNA10,LRRC10,GREM2,OR6N1,CAPN8,TFF3,OR4K5,HOPX,COMP,OR4A5,OR5AN1,KRTAP1-3,OR5AS1,GABRR2,OR13G1,OR2M5,HTR3A,KRTAP13-3,OR13C5,OR4C3,CHST8,MAS1,OR52L1,KRTAP4-2,OR8K1,KIRREL3,OR6B2,KRTAP19-1,KRTAP3-1,KRTAP3-2,KRTAP9-9,OR56A4,PSMA6,OR5B17,TMEM108,OR51A2,P2RX5,OR5T1,OR1A1,OR13C8,OR13C2,GAP43,MFAP5,ADAMTSL1,OR51B4,LCE1F,KCNQ2,SFRP4,OR2AG2,OR2M7,OR51L1,OR5H1,CRLF1,KRTAP21-2,OR8G1,OR6K6,KRTAP19-2,OR10Z1,KRTAP10-1,DNAH11,NPTX2,OR4K1,OR5T2,EDARADD,PI16,JPH2,INSC,FN1,ACTBL2,C1QL1,NPFF,OR2A12,BEND6,OR1L8,HBD,OR1J2,TAS2R60,VSIG4,IGF2BP3,CHRNA10,OR5AP2,OR52K1,CYP26B1,FAT3,IL10,TNFRSF11A,GCGR,OR9A2,LCN2,TOP2A,MESP2,CDH22,OR10A5,OR4C46,UCHL1,FGL1,ACTC1,VASP,CIT,CTNNA3,OR52W1,IL5RA,SOSTDC1,TTC8,RADIL,TAS2R8,NTN1,OR52E6,P2RX6,CTNNA2,TTN,OR6K3,MUSTN1,OR11H2,CCR2,P2RY12,CNN1,HRC,PTGS2,DEF8,APOC1,LYZ,GLP1R,NDRG4,CNGA4,APOC2,KRTAP5-1,HADH,SERPINA3,OR52D1,TMEM178A,EFNA4,PIR,HSD17B3,PTGFR,SCRG1,NR6A1,LGI2,AKR1C2,CDH23,ADAMTS2,P2RY1,IGSF11,TSHZ3,PDLIM3,CRYGS,KIF20B,ESR1,ARHGAP22,AGAP2,CYP4F12,SLC26A7,TFCP2L1,RELT,MAP1A,LOXL1,KIF18A,PRICKLE4,JMJD6,ARG2,POU5F1,ROBO1,ALOX5,ANLN,CDK1,SELPLG,GREB1,MYH11,ABCB1,CYP2J2,VAV3,TYMS,SCN1B,MATN3,LAMB3,SRD5A1,SRPX2,S

						GIP1,GLG1,TPM2,SIX2,SAMHD1
GO:0071944	CC	cell periphery	1.40E-07	6.853891822	186	HAPLN4,CSNK1G1,IGLL5,PLCH2,SLCO1A2,DMBT1,RGS16,PREX1,LRFN2,NRG3,LRRTM3,GABRA2,NTNG2,GLRA1,DGKG,OR10J3,SLC6A17,OR4F5,SLC18A2,SLC26A9,OR6C74,UNC5A,OR5L1,OR4D2,KCNG3,SLC27A6,OR2T33,CLDN25,OR2T6,ADAM30,CDHR1,GJA10,RASD1,TAAR9,OR8H2,INSRR,POSTN,OR4N2,OR2A25,LY6G6E,TAS2R7,KIF20A,OR1E2,OR2B3,SLC45A3,OR6N1,OR4K5,COMP,OR4A5,OR5AN1,OR5AS1,GABRR2,OR13G1,OR2M5,HTR3A,OR13C5,OR4C3,MAS1,OR52L1,OR8K1,KIRREL3,OR6B2,SLCO5A1,OR56A4,OR5B17,PCDH7,OR51A2,P2RX5,SLC22A9,OR5T1,OR1A1,OR13C8,OR13C2,GAP43,MFAP5,ADAMTSL1,OR51B4,KCNQ2,KCNF1,OR2AG2,CD1E,OR2M7,OR51L1,OR5H1,CRLF1,OR8G1,OR6K6,OR10Z1,KCNH1,OR4K1,OR5T2,SDR16C5,JPH2,INSC,FN1,OR2A12,CAPNS2,YIPF4,OR1L8,OR1J2,TAS2R60,CHRNA10,OR5AP2,MEP1B,OR52K1,FAT3,TNFRSF11A,GCGR,OR9A2,ENTPD3,OXGR1,CDH22,OR10A5,OR4C46,UCHL1,HLA-C,CLEC4D,FGL1,VASP,OR52W1,IL5RA,TTC8,TAS2R8,OLFM4,TSPAN1,GPR141,NTN1,OR52E6,P2RX6,CTNNA2,TTN,OR6K3,OR11H2,CCR2,PRAM1,P2RY12,PTGS2,ITGBL1,GLP1R,NDRG4,KLRK1,CNGA4,SERPINA3,OR52D1,EFNA4,PTGFR,CFB,FCHO1,LRRC7,MMP28,CDH23,ADAMTS2,ATP2C1,P2RY1,IGSF11,TSHZ3,FRMPD1,SELL,ESR1,CYP4F12,RASD2,SLC26A7,LY6G5B,CSF2RA,RELT,LOXL1,KIF18A,B3GNT3,MYO1F,JMJD6,ROBO1,ANLN,SELPLG,ABCB1,DLG2,ADAMTS10,VAV3,SCN1B,LAT,MATN3,LAMB3,SRPX2,SGIP1,SLC7A7,GLG1,SAMHD1
GO:0005886	CC	plasma membrane	9.39E-07	6.027126436	171	CSNK1G1,IGLL5,PLCH2,SLCO1A2,RGS16,PREX1,LRFN2,NRG3,LRRTM3,GABRA2,NTNG2,GLRA1,DGKG,OR10J3,SLC6A17,OR4F5,SLC18A2,SLC26A9,OR6C74,UNC5A,OR5L1,OR4D2,KCNG3,SLC27A6,OR2T33,CLDN25,OR2T6,ADA

						M30,CDHR1,GJA10,RASD1,TAAR9,OR8H2,INSRR,OR4N2,OR2A25,LY6G6E,TAS2R7,KIF20A,OR1E2,OR2B3,SLC45A3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,GABRR2,OR13G1,OR2M5,HTR3A,OR13C5,OR4C3,MAS1,OR52L1,OR8K1,KIRREL3,OR6B2,SLCO5A1,OR56A4,OR5B17,PCDH7,OR51A2,P2RX5,SLC22A9,OR5T1,OR1A1,OR13C8,OR13C2,GAP43,ADAMTSL1,OR51B4,KCNQ2,KCNF1,OR2AG2,CD1E,OR2M7,OR51L1,OR5H1,CRLF1,OR8G1,OR6K6,OR10Z1,KCNH1,OR4K1,OR5T2,SDR16C5,JPH2,INSC,FN1,OR2A12,CAPNS2,YIPF4,OR1L8,OR1J2,TAS2R60,CHRNA10,OR5AP2,MEP1B,OR52K1,FAT3,TNFRSF11A,GCGR,OR9A2,ENTPD3,OXGR1,CDH22,OR10A5,OR4C46,UCHL1,HLA-C,CLEC4D,VASP,OR52W1,IL5RA,TTC8,TAS2R8,OLFM4,TSPAN1,GPR141,OR52E6,P2RX6,CTNNA2,TTN,OR6K3,OR11H2,CCR2,PRAM1,P2RY12,PTGS2,ITGBL1,GLP1R,NDRG4,KLRK1,CNGA4,OR52D1,EFNA4,PTGFR,CFB,FCHO1,LRRC7,CDH23,ATP2C1,P2RY1,IGSF11,TSHZ3,FRMPD1,SELL,ESR1,CYP4F12,RASD2,SLC26A7,LY6G5B,CSF2RA,RELT,KIF18A,B3GNT3,MYO1F,JMJD6,ROBO1,SELPLG,ABCB1,DLG2,VAV3,SCN1B,LAT,SRPX2,SGIP1,SLC7A7,GLG1,SAMHD1
GO:0004888	MF	transmembranesignaling receptor activity	4.64E-19	18.3338049	83	GABRA2,GLRA1,OR10J3,OR4F5,OR6C74,UNC5A,OR5L1,OR4D2,OR2T33,OR2T6,TAAR9,OR8H2,INSRR,OR4N2,OR2A25,TAS2R7,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,GABRR2,OR13G1,OR2M5,HTR3A,OR13C5,OR4C3,MAS1,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,P2RX5,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,CRLF1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,OR2A12,OR1L8,OR1J2,TAS2R60,CHRNA10,OR5AP2,OR52K1,TNFRSF11A,GCGR,OR9A2,OXGR1,OR10A5,OR4C46,OR52W1,IL5RA,SOSTDC1,TAS2R8,GPR141,OR52E6,P2RX6,OR6K3,OR11H2,CCR2,P2RY12,GLP1R,OR52D1,EFNA4

						,PTGFR,P2RY1,CSF2RA,ROBO1
GO:0060089	MF	molecular transducer activity	2.72E-18	17.56616903	88	DMBT1,GABRA2,GLRA1,OR10J3,RXRG,OR4F5,OR6C74,UNC5A,OR5L1,OR4D2,OR2T33,OR2T6,TAAR9,OR8H2,INSRR,OR4N2,OR2A25,TAS2R7,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,GABRR2,OR13G1,OR2M5,HTR3A,OR13C5,OR4C3,MAS1,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,P2RX5,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,CRLF1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,OR2A12,OR1L8,OR1J2,TAS2R60,CHRNA10,OR5AP2,OR52K1,TNFRSF11A,GCGR,OR9A2,OXGR1,OR10A5,OR4C46,OR52W1,IL5RA,SOSTDC1,TAS2R8,GPR141,OR52E6,P2RX6,OR6K3,OR11H2,CCR2,P2RY12,GLP1R,KLRK1,OR52D1,EFNA4,PTGFR,P2RY1,ESR1,CSF2RA,JMJD6,ROBO1

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

Pathway ID	**Pathway Name**	**Adjusted p value**	**Negative log10 of adjusted p value**	**Gene Count**	**Gene**
		Up regulated genes			
REAC:R-HSA-5663202	Diseases of signal transduction by growth factor receptors and second messengers	0.002918856	2.534787284	25	FGA,FGB,FGG,HEYL,HRAS,MYC,IRS1,KIAA1549,STAT1,SYVN1,TCF7L2,DLL4,SOS1,EGFR,PIK3CA,NCSTN,MAML1,MAPK3,TRIM24,ETV6,GSK3A,RNF43,HSP90AA1,GAB1,TNKS
REAC:R-HSA-6809371	Formation of the cornified envelope	0.009712336	2.012676308	12	KRT6A,LCE3D,SPRR3,FLG,SPRR2D,SPRR1B,SPRR1A,KRT16,KRT13,SPRR2E,LCE3E,KLK13
REAC:R-HSA-156827	L13a-mediated translational silencing of Ceruloplasmin expression	0.027095018	1.567110554	10	RPS6,RPL8,RPS28,EIF4B,RPL18,EIF3B,RPL18A,RPS15,RPL39,RPL19
REAC:R-HSA-1643685	Disease	0.027095018	1.567110554	60	CGA,FGA,FGB,FGG,CALCR,ABCB11,MUC21,GCG,ADAMTS8,PTGER4,GPC6,ABCC9,RPS6,SLC29A3,RPL8,HEYL,HRAS,SFTPD,MYC,IRS1,RPS28,MUC6,NUP205,WASF1,PAPSS2,KIAA1549,IL6R,ABCA1,RPL18,STAT1,FMOD,ARPC1A,SYVN1,TCF7L2,DLL4,ELK1,SOS1,PRKACA,EGFR,PIK3CA,NCSTN,MAML1,MAPK3,RPL18A,RPS15,TRIM24,PRKCSH,ETV6,GSK3A,MAOA,RNF43,HSP90AA1,GAB1,S1PR1,RPL39,TNKS,NFKBIA,RPL19,SLC39A4,BSG
REAC:R-HSA-9006934	Signaling by Receptor Tyrosine Kinases	0.03209698	1.493535827	25	IGF2,EGR1,COL6A3,VEGFC,ID3,EGR3,HRAS,IRS1,WASF1,DUSP4,STAT1,ELK1,PTBP1,SOS1,PRKACA,EGFR,PIK3CA,NCSTN,MAPK3,RAB4A,STUB1,HSP90AA1,GAB1,

					INSR,RALB
REAC:R-HSA-1266738	Developmental Biology	0.032172975	1.492508778	45	KRT6A,LCE3D,SPRR3,FLG,SPRR2D,SPRR1B,SPRR1A,DCC,KRT16,ZSCAN10,KRT13,SPRR2E,LCE3E,COL6A3,MPZ,KLK13,RPS6,RPL8,HRAS,MYC,RPS28,IL6R,PBX1,RPL18,ARPC1A,HELZ2,SOS1,PRKACA,EGFR,PIK3CA,MED13L,NCSTN,MAML1,MAPK3,RPL18A,ACVR2B,RPS15,HSP90AA1,GAB1,RPL39,MED25,CASC3,SIAH2,RNPS1,RPL19
Down regulated genes					
REAC:R-HSA-381753	Olfactory Signaling Pathway	4.32E-23	22.36427935	54	OR10J3,OR4F5,OR6C74,OR5L1,OR4D2,OR2T33,OR2T6,OR8H2,OR4N2,OR2A25,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,OR13G1,OR2M5,OR13C5,OR4C3,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,OR2A12,OR1L8,OR1J2,OR5AP2,OR52K1,OR9A2,OR10A5,OR4C46,OR52W1,OR52E6,OR6K3,OR11H2,OR52D1
REAC:R-HSA-9709957	Sensory Perception	4.85E-21	20.31389969	57	OR10J3,OR4F5,OR6C74,OR5L1,OR4D2,OR2T33,OR2T6,OR8H2,OR4N2,OR2A25,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,OR13G1,OR2M5,OR13C5,OR4C3,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,OR2A12,OR1L8,RDH16,OR1J2,OR5AP2,OR52K1,OR9A2,OR10A5,OR4C46,OR52W1,OR52E6,OR6K3,BCO2,OR11H2,APOC2,OR52D1
REAC:R-HSA-418555	G alpha (s) signalling events	6.29E-20	19.20156126	58	IAPP,ADCYAP1,OR10J3,OR4F5,OR6C74,OR5L1,OR4D2,OR2T33,OR2T6,TAAR9,OR8H2,OR4N2,OR2A25,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,OR13G1,OR2M5,OR13C5,OR4C3,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,OR2A12,OR1L8,OR1J2,OR5AP2,OR52K1,OR9A2,OR10A5,OR4C46,OR52W1,OR52E6,OR6K3,OR11H2,GLP1R,OR52D1
REAC:R-HSA-388396	GPCR downstream signalling	9.32E-15	14.0308131	76	IAPP,ADCYAP1,RGS16,PREX1,DGKG,OR10J3,OR4F5,OR6C74,OR5L1,OR4D2,ARHGEF35,OR2T33,OR2T6,TAAR9,OR8H2,OR4N2,OR2A25,TAS2R7,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,OR13G1,OR2M5,OR13C5,OR4C3,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,NPFF,OR2A12,OR1L8,RDH16,OR1J2,TAS2R60,OR5AP2,OR52K1,OR9A2,OXGR1,OR10A5,OR4C46,OR52W1,TAS2R8,OR52E6,OR6K3,BCO2,OR11H2,CCR2,P2RY12,GLP1R,APOC2,OR52D1,PTGFR,P2RY1,PDE1C,VAV3
REAC:R-HSA-372790	Signaling by GPCR	2.45E-13	12.61114695	76	IAPP,ADCYAP1,RGS16,PREX1,DGKG,OR10J3,OR4F5,OR6C74,OR5L1,OR4D2,ARHGEF35,OR2T33,OR2T6,TAAR9,OR8H2,

					OR4N2,OR2A25,TAS2R7,OR1E2,OR2B3,OR6N1,OR4K5,OR4A5,OR5AN1,OR5AS1,OR13G1,OR2M5,OR13C5,OR4C3,OR52L1,OR8K1,OR6B2,OR56A4,OR5B17,OR51A2,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,NPFF,OR2A12,OR1L8,RDH16,OR1J2,TAS2R60,OR5AP2,OR52K1,OR9A2,OXGR1,OR10A5,OR4C46,OR52W1,TAS2R8,OR52E6,OR6K3,BCO2,OR11H2,CCR2,P2RY12,GLP1R,APOC2,OR52D1,PTGFR,P2RY1,PDE1C,VAV3
REAC:R-HSA-162582	Signal Transduction	7.38146E-05	4.131857963	105	IAPP,ADCYAP1,RGS16,PREX1,NRG3,DLK1,DGKG,OR10J3,RXRG,OR4F5,OR6C74,DKK4,OR5L1,OR4D2,ARHGEF35,OR2T33,OR2T6,TAAR9,OR8H2,OR4N2,OR2A25,TAS2R7,OR1E2,OR2B3,GREM2,OR6N1,TFF3,OR4K5,OR4A5,OR5AN1,OR5AS1,OR13G1,OR2M5,OR13C5,OR4C3,OR52L1,OR8K1,OR6B2,OR56A4,PSMA6,DLGAP5,OR5B17,OR51A2,OR5T1,OR1A1,OR13C8,OR13C2,OR51B4,OR2AG2,OR2M7,OR51L1,OR5H1,OR8G1,OR6K6,OR10Z1,OR4K1,OR5T2,SDR16C5,FN1,NPFF,OR2A12,OR1L8,RDH16,OR1J2,TAS2R60,OR5AP2,OR52K1,CYP26B1,OR9A2,OXGR1,OR10A5,SPC24,OR4C46,CIT,OR52W1,IL5RA,TAS2R8,OR52E6,OR6K3,BCO2,OR11H2,CCR2,P2RY12,APOC1,GLP1R,APOC2,OR52D1,SMAD9,PTGFR,BUB1B,P2RY1,ARHGAP20,NEDD8,ESR1,ARHGAP22,CSF2RA,KIF18A,ARHGAP9,CDK1,GREB1,MYH11,PDE1C,DLG2,VAV3,LAMB3

Table 5 Topology table for up and down regulated genes.

Regulation	Node	Degree	Betweenness	Stress	Closeness
Up	MYC	769	0.24506	1.04E+08	0.402932
Up	EGFR	469	0.138032	61812344	0.381322
Up	LNX1	301	0.098028	35639540	0.344753
Up	YBX1	242	0.052423	15440248	0.370488
Up	HSP90AA1	198	0.042012	18645766	0.349323
Up	RNPS1	148	0.029398	16186898	0.324119
Up	SGTA	139	0.039126	11319544	0.315439
Up	TNFRSF1A	116	0.016842	8191032	0.328598
Up	SQSTM1	112	0.025913	6213766	0.344335
Up	MAST3	105	0.022	12287012	0.305669
Up	POU6F2	99	0.028224	4939174	0.317338
Up	STUB1	95	0.01869	5557470	0.333856
Up	FKBP5	94	0.015263	3991284	0.329764
Up	PRMT6	82	0.023047	4016020	0.301486
Up	MAPK3	78	0.01798	4710364	0.312259
Up	SMAD1	77	0.014129	5216492	0.309237
Up	TFAP2C	77	0.020062	3309460	0.333573
Up	NCL	73	0.015947	5344646	0.374917
Up	ETS1	69	0.014065	3895426	0.310987
Up	MEX3C	68	0.003769	2594352	0.310439
Up	ACD	66	0.014094	3525238	0.307138
Up	NFKBIA	66	0.008138	4939524	0.310854
Up	GAB1	61	0.005759	2357788	0.296365
Up	ZNF581	58	0.008074	2392056	0.303509
Up	PRKACA	58	0.012141	2683394	0.312833
Up	KRT13	56	0.009539	2356276	0.31577
Up	SF3A1	54	0.005297	3631052	0.304231
Up	STAT1	54	0.010129	1749810	0.330531

Up	ATF7IP	54	0.011319	2610676	0.297746
Up	FOXK1	52	0.010322	2431366	0.309968
Up	KRT16	52	0.009137	2768286	0.302646
Up	RPS6	50	0.005709	1809230	0.323503
Up	IFIT3	48	0.004333	1419676	0.307396
Up	UBE2E2	48	0.009384	2778786	0.289714
Up	PKN1	47	0.007325	2119206	0.29714
Up	ARL6IP1	46	0.011853	5167578	0.284047
Up	UTP14A	45	0.00788	1716012	0.322239
Up	PRPF8	44	0.006824	1731078	0.329977
Up	GADD45G	44	0.007648	1727574	0.29879
Up	ATP13A2	43	0.011364	3235048	0.28605
Up	HRAS	42	0.006113	1934688	0.306916
Up	DCC	42	0.005613	2081812	0.292265
Up	SUN2	42	0.004561	2137880	0.299806
Up	DYSF	41	0.007116	2286238	0.293962
Up	NCSTN	40	0.007729	5776106	0.274308
Up	RPL8	37	0.004561	1421422	0.324922
Up	BACH2	37	0.008838	2796552	0.273369
Up	PIK3CA	37	0.005768	1280756	0.304576
Up	PTBP1	36	0.003339	1190818	0.333507
Up	FKBP8	35	0.00586	1371274	0.3223
Up	NES	35	0.007013	1126640	0.295338
Up	KRT6A	34	0.005784	1381296	0.320281
Up	NUP205	33	0.005495	1090580	0.323442
Up	FOXP1	33	0.006278	1144548	0.31992
Up	INSR	33	0.003132	1562024	0.279757
Up	BCAP31	32	0.00482	1838970	0.292131
Up	BTF3	31	0.00454	1476600	0.290636
Up	RPL18A	31	0.002498	754566	0.318306
Up	KIAA0408	30	0.00425	1221042	0.302575
Up	USP1	30	0.004591	2441058	0.280879
Up	EIF3B	29	0.003846	916674	0.315848
Up	HSPA2	28	0.002862	684442	0.313947
Up	RPS28	28	0.002873	1278818	0.301718
Up	SOS1	28	0.002513	879664	0.284205
Up	ERRFI1	26	0.002199	611152	0.311214
Up	LCE3E	26	0.001327	524110	0.25448
Up	GSK3A	26	0.004252	1655588	0.292867
Up	NAT10	26	0.001696	666842	0.325191
Up	LIG3	26	0.00228	725644	0.294691
Up	RPL18	25	9.73E-04	477540	0.322646
Up	SLC1A5	25	0.004674	807018	0.306677
Up	EIF4B	25	0.00188	620280	0.295594
Up	NEDD9	24	0.003127	549922	0.289271
Up	CASC3	23	0.002491	601190	0.302503
Up	FOSL2	23	0.003682	831006	0.310911
Up	SMURF1	22	0.002704	664080	0.284142
Up	PLOD3	22	0.003554	1082282	0.335808
Up	TCOF1	22	0.00218	501286	0.314295
Up	ZNF326	22	0.001349	640724	0.29001
Up	SP4	22	0.003993	853624	0.26749
Up	EGR1	21	0.002422	466912	0.302056
Up	MAGEA2	21	0.004402	1011862	0.293759
Up	CREB3L1	21	0.006704	4786040	0.227129
Up	WASF1	20	0.003044	1067564	0.274868
Up	IRS1	20	0.001568	411892	0.309837
Up	CRTC3	20	0.002135	967284	0.279558
Up	FBP2	20	9.48E-04	423694	0.288846
Up	MED25	20	0.001218	294794	0.275609
Up	LCE3D	20	4.82E-04	304904	0.263329
Up	DEAF1	19	0.002531	618844	0.3017
Up	PDK3	19	0.003011	604606	0.307526
Up	RPL19	19	6.37E-04	392064	0.319241
Up	ABCA1	19	0.004473	1062228	0.298441
Up	SAE1	19	0.003167	702666	0.299157
Up	MAL	19	0.004533	1470896	0.264227
Up	RAB4A	19	0.003857	747204	0.292398
Up	RALB	19	0.001738	1634506	0.255536
Up	TRAPPC3	19	0.005096	1890182	0.252046

Up	DPP4	19	0.00527	1619646	0.234023
Up	PRKCSH	18	0.002123	375070	0.316043
Up	RBM22	18	0.002051	950490	0.283386
Up	CAMSAP3	18	0.002085	1031300	0.274014
Up	AK1	18	0.002632	1174620	0.257986
Up	TTI1	17	0.001947	994560	0.275505
Up	RUNX1T1	17	0.002454	1455104	0.275046
Up	RPS15	16	0.00225	468552	0.316395
Up	NR0B2	16	0.002709	597146	0.313581
Up	POLR1D	16	0.001752	656232	0.282369
Up	FAM83B	16	8.49E-04	301500	0.277314
Up	PBX1	16	0.001944	703560	0.258718
Up	TCF7L2	15	0.001345	373312	0.28326
Up	BCOR	15	0.002336	806128	0.273164
Up	ID3	15	0.002818	819716	0.269962
Up	SLC35E1	15	0.003323	1409720	0.24654
Up	TPI1	14	0.002071	457522	0.314391
Up	SIAH2	14	0.001994	845214	0.269677
Up	TNKS	14	0.002475	650184	0.251959
Up	RBM23	14	2.87E-04	166572	0.276758
Up	HEYL	14	0.002211	402860	0.280864
Up	MRPL37	2	1.61E-04	51382	0.28108
Up	GID8	2	4.01E-05	6218	0.246921
Up	DIP2B	2	0	0	0.291299
Up	SH3RF1	2	2.53E-04	99400	0.287919
Up	ZFP36L1	2	9.45E-05	13940	0.255792
Up	GCG	2	1.27E-04	41870	0.209131
Up	YIPF3	2	7.28E-05	18416	0.211048
Up	FGB	1	0	0	0.254404
Up	FAM20C	1	0	0	0.254404
Up	GLI3	1	0	0	0.236207
Up	NXN	1	0	0	0.215614
Up	PHLDA1	1	0	0	0.276071
Up	SPRR1A	1	0	0	0.276071
Up	DNAJC4	1	0	0	0.276071
Up	MRPL49	1	0	0	0.270347
Up	COL6A3	1	0	0	0.22719
Up	MZT2B	1	0	0	0.287223
Up	ZFHX3	1	0	0	0.287223
Up	SNX19	1	0	0	0.287223
Up	KLF10	1	0	0	0.287223
Up	ST6GALNAC6	1	0	0	0.287223
Up	RPRD2	1	0	0	0.287223
Up	ETV6	1	0	0	0.287223
Up	SYVN1	1	0	0	0.273764
Up	SPRR2D	1	0	0	0.229084
Up	FGF21	1	0	0	0.239809
Up	TMEM174	1	0	0	0.239809
Up	CYGB	1	0	0	0.222435
Up	CRNN	1	0	0	0.256151
Up	PLCE1	1	0	0	0.258901
Up	SFTPD	1	0	0	0.201125
Up	TRIM24	1	0	0	0.273179
Up	APOD	1	0	0	0.273179
Up	THRB	1	0	0	0.21607
Up	IKZF4	1	0	0	0.23715
Up	SPRR3	1	0	0	0.23715
Up	CNTNAP4	1	0	0	0.23412
Up	ZNRF1	1	0	0	0.224644
Up	ATXN7L1	1	0	0	0.211048
Up	FLG	1	0	0	0.219296
Up	MT2A	1	0	0	0.250147
Up	SHISA5	1	0	0	0.250147
Up	RWDD2B	1	0	0	0.230063
Up	OAS1	1	0	0	0.231658
Up	TMED5	1	0	0	0.231658
Up	NR1D2	1	0	0	0.231658
Up	GPATCH4	1	0	0	0.228011
Up	KLF11	1	0	0	0.217829
Up	ZFP36	1	0	0	0.239696

Up	MTMR3	1	0	0	0.239696
Up	FOXN3	1	0	0	0.239696
Up	PGAP2	1	0	0	0.221817
Up	ELK1	1	0	0	0.237967
Up	DUSP1	1	0	0	0.237967
Up	IL6ST	1	0	0	0.248433
Up	SNX12	1	0	0	0.221222
Up	LSM11	1	0	0	0.237183
Up	MED13L	1	0	0	0.232501
Down	ESR1	448	0.115717	68567806	0.375827
Down	FN1	445	0.130416	47618446	0.393806
Down	TK1	155	0.044276	10622930	0.341187
Down	ANLN	102	0.019831	5950428	0.327945
Down	SMAD9	99	0.023512	10495428	0.31337
Down	NEDD8	94	0.013216	4708022	0.323626
Down	TTN	88	0.021791	4877390	0.354606
Down	CDK1	76	0.019122	4123802	0.343387
Down	KRTAP4-2	73	0.019925	3654538	0.300106
Down	MED10	65	0.012717	3973710	0.302915
Down	EXOSC8	61	0.015702	2371472	0.315244
Down	NEK6	61	0.009473	2973110	0.31289
Down	OIP5	60	0.013758	3810166	0.30688
Down	PSMA6	57	0.012284	2937164	0.324778
Down	BUB1B	54	0.010813	5323030	0.298111
Down	FOXM1	43	0.007242	2131654	0.300317
Down	RPL31	35	0.003717	1156016	0.323013
Down	EEF1A2	33	0.002074	927396	0.307212
Down	JMJD6	31	0.006976	4154054	0.261751
Down	VASP	30	0.005691	1017020	0.316768
Down	MAP3K8	30	0.001715	773154	0.310458
Down	UCHL1	28	0.003224	905164	0.308808
Down	TOP2A	28	0.0032	1042178	0.328788
Down	MYH11	28	0.003406	1173838	0.305103
Down	RASSF1	27	0.004112	1253252	0.299175
Down	KRTAP3-2	27	0.004532	1398432	0.265421
Down	TXNDC9	26	0.004126	1143166	0.278477
Down	ACTC1	24	0.004063	1053202	0.329594
Down	SPC24	23	0.002762	801496	0.268982
Down	SH3BP2	21	0.001863	813564	0.277887
Down	IGF2BP3	20	0.001318	388432	0.332401
Down	KIF20A	20	0.004794	850452	0.262706
Down	SFRP4	20	0.001565	724830	0.277404
Down	KIF20B	18	0.003465	529620	0.306935
Down	RASD1	18	0.001969	611526	0.282869
Down	NEFM	18	0.002405	500776	0.29515
Down	RADIL	18	0.001925	718708	0.28187
Down	LCE1F	18	5.31E-04	1078996	0.215551
Down	LUC7L	17	0.001779	331232	0.297175
Down	LYZ	17	0.002823	462382	0.311441
Down	PFKFB2	17	0.002624	984686	0.285029
Down	ACTBL2	17	5.95E-04	248094	0.310647
Down	FCHO1	17	0.002083	725112	0.267588
Down	KIF18A	17	0.002914	1632588	0.264802
Down	SAMHD1	16	0.002408	964652	0.269962
Down	LAT	15	0.002067	607316	0.301593
Down	PBK	15	0.002668	669380	0.294912
Down	TPX2	15	9.04E-04	407858	0.293506
Down	RRM2	15	0.002347	419566	0.272147
Down	LAMB3	15	0.002279	1460718	0.265531
Down	ALOX5	15	0.003126	496364	0.267099
Down	TPM2	15	4.76E-04	162954	0.290092
Down	IP6K3	14	0.001497	346042	0.275387
Down	VAV3	14	0.001429	470180	0.297573
Down	NDUFA8	13	0.00167	479156	0.290455
Down	BIRC8	13	0.002152	927372	0.24679
Down	DLG2	13	0.002105	767688	0.273896
Down	MYCN	12	1.11E-04	41976	0.304939
Down	PRAM1	12	0.001039	343780	0.260883
Down	PCDH7	12	0.001704	788890	0.266375
Down	EDARADD	11	0.001215	325252	0.268544

Down	GREB1	11	9.15E-04	206196	0.268968
Down	ZNF622	11	8.30E-04	730808	0.269663
Down	RXRG	11	0.002054	800986	0.250012
Down	GLP1R	11	3.87E-04	306068	0.257778
Down	TTC8	11	0.003532	958578	0.227362
Down	SERPINA3	10	0.002011	543412	0.243151
Down	CDK15	10	2.37E-04	85694	0.294623
Down	HLA-DQA1	10	0.001488	682934	0.249878
Down	HSD17B3	10	1.13E-04	75794	0.26087
Down	TSHZ3	10	0.001111	304690	0.256253
Down	MAP1A	9	8.61E-04	207068	0.312393
Down	CSNK1G1	9	0.001614	637430	0.248529
Down	GTF2H2C	9	0.001734	341202	0.245876
Down	PDLIM3	9	0.001957	559870	0.239831
Down	WDR3	9	6.45E-04	234640	0.274455
Down	TNFAIP8	9	9.44E-04	850962	0.230957
Down	ADAMTS10	8	9.45E-04	260474	0.258443
Down	ABCB1	8	9.74E-04	146904	0.3
Down	QRICH2	8	0.001291	295070	0.261336
Down	INS	8	4.75E-04	194074	0.248216
Down	COMP	8	0.001207	326670	0.231995
Down	SHCBP1	7	4.46E-04	233846	0.256678
Down	DLGAP5	7	1.46E-04	74806	0.290108
Down	ARHGAP9	7	3.62E-04	66924	0.28522
Down	KCNH1	7	3.41E-04	213892	0.253094
Down	KLHL1	6	1.15E-04	30788	0.283638
Down	LCN2	6	4.47E-04	83350	0.256575
Down	TYMS	6	4.58E-04	134624	0.25317
Down	CDKN1C	6	4.20E-04	155814	0.26589
Down	DMBT1	6	0.001176	361022	0.251748
Down	SULT1C2	6	4.34E-04	98520	0.244289
Down	IL10	6	8.05E-04	231670	0.245675
Down	SAMD3	6	6.69E-04	135970	0.268713
Down	NCKAP5	6	4.03E-05	22814	0.2639
Down	CNN1	6	2.65E-04	64314	0.23624
Down	PREX1	6	8.35E-04	387030	0.254975
Down	CTNNA2	5	5.71E-04	182504	0.281204
Down	POU5F1	5	7.40E-04	107680	0.274839
Down	POSTN	5	5.96E-04	207158	0.228766
Down	CSF2RA	5	8.10E-04	258390	0.252907
Down	MATN3	5	1.69E-04	28890	0.235848
Down	ASB9	5	5.76E-04	238362	0.238055
Down	KRTAP5-1	5	0.001174	179682	0.190051
Down	IL5RA	5	0.001176	281872	0.257441
Down	KANK4	5	7.94E-04	141232	0.240633
Down	ASB16	5	2.41E-05	16592	0.266028
Down	KIF4A	5	4.60E-05	13994	0.259374
Down	ROBO1	5	4.93E-04	116624	0.246421
Down	TNFRSF11A	4	4.04E-04	116804	0.251934
Down	KRTAP3-1	4	2.89E-05	20452	0.252494
Down	UBXN10	4	5.63E-04	69202	0.248047
Down	GLG1	4	4.17E-04	62018	0.265572
Down	LOXL1	4	4.78E-04	74588	0.250404
Down	COMMD7	4	4.03E-04	180366	0.233127
Down	SELPLG	4	8.09E-04	244340	0.221136
Down	YIPF4	4	4.79E-05	15522	0.197986
Down	TMEM108	4	2.77E-05	10972	0.243081
Down	KRTAP13-3	3	3.50E-07	422	0.210396
Down	LRRC7	3	7.82E-04	166682	0.180159
Down	GPX2	2	0	0	0.299578
Down	CDH23	1	0	0	0.215614
Down	ISX	1	0	0	0.240905
Down	NPTX2	1	0	0	0.287223
Down	KCNG3	1	0	0	0.287223
Down	SMIM5	1	0	0	0.239809
Down	TFF3	1	0	0	0.239809
Down	FAM111B	1	0	0	0.222435
Down	CDKN3	1	0	0	0.255626
Down	IFI27L2	1	0	0	0.250147
Down	NTN1	1	0	0	0.226175

Down	AGAP2	1	0	0	0.218611
Down	PIR	1	0	0	0.238611
Down	RNASE2	1	0	0	0.215016
Down	ADCYAP1	1	0	0	0.189649
Down	HADH	1	0	0	0.248433
Down	NDRG4	1	0	0	0.221222

Table 6 miRNA - target gene and TF - target gene interaction

Regulation	Target Genes	Degree	MicroRNA	Regulation	Target Genes	Degree	TF
Up	MYC	194	hsa-mir-4677-3p	Up	MAPK3	48	JUND
Up	HSP90AA1	188	hsa-mir-3125	Up	HSP90AA1	35	HSF2
Up	FKBP5	116	hsa-mir-4779	Up	SQSTM1	34	SMAD4
Up	RNPS1	109	hsa-mir-548az-3p	Up	STUB1	31	ATF6
Up	SQSTM1	108	hsa-mir-106a-5p	Up	EGFR	27	ELF3
Up	EGFR	83	hsa-mir-219a-5p	Up	YBX1	24	TFAP2A
Up	MAST3	76	hsa-mir-129-2-3p	Up	LNX1	21	MAX
Up	YBX1	48	hsa-mir-1537-3p	Up	FKBP5	20	PGR
Up	PRMT6	43	hsa-mir-4330	Up	PRMT6	9	YY1
Up	MAPK3	33	hsa-mir-3158-3p	Up	SGTA	7	MXI1
Up	SGTA	24	hsa-mir-421	Up	POU6F2	7	ALX1
Up	TNFRSF1A	22	hsa-mir-548an	Up	RNPS1	7	STAT3
Up	STUB1	16	hsa-mir-942-5p	Up	TNFRSF1A	6	EP300
Up	POU6F2	15	hsa-mir-7850-5p	Up	MAST3	1	NFYA
Down	ANLN	127	hsa-mir-664a-3p	Down	ESR1	126	FOXF2
Down	CDK1	109	hsa-mir-5688	Down	SMAD9	38	XAB2
Down	FN1	105	hsa-mir-199b-3p	Down	CDK1	36	KHDRBS1
Down	ESR1	98	hsa-mir-206	Down	FN1	25	RELA
Down	TK1	80	hsa-mir-6512-3p	Down	NEK6	16	SRY
Down	OIP5	62	hsa-mir-767-5p	Down	TK1	11	DRAP1
Down	SMAD9	58	hsa-mir-3689a-3p	Down	NEDD8	10	PARP1
Down	MED10	41	hsa-mir-647	Down	TTN	10	FOXD3
Down	NEK6	34	hsa-mir-4485-3p	Down	ANLN	9	JUN
Down	BUB1B	32	hsa-mir-449b-5p	Down	BUB1B	9	MYB
Down	TTN	31	hsa-mir-181c-5p	Down	MED10	6	KDM4B
Down	NEDD8	26	hsa-mir-583	Down	PSMA6	6	EBF1
Down	PSMA6	17	hsa-mir-539-5p	Down	OIP5	5	GATA2
Down	EXOSC8	17	hsa-mir-191-5p	Down	KRTAP4-2	1	TBP

Figures

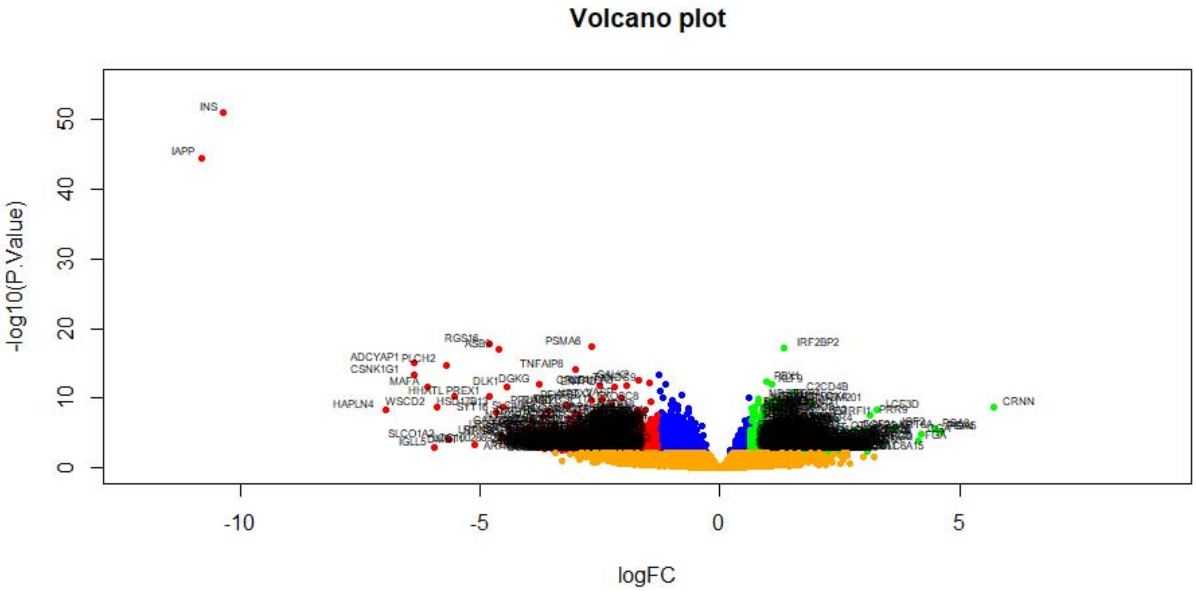

Fig. 1. Volcano plot of differentially expressed genes. Genes with a significant change of more than two-fold were selected. Green dot represented up regulated significant genes and red dot represented down regulated significant genes.

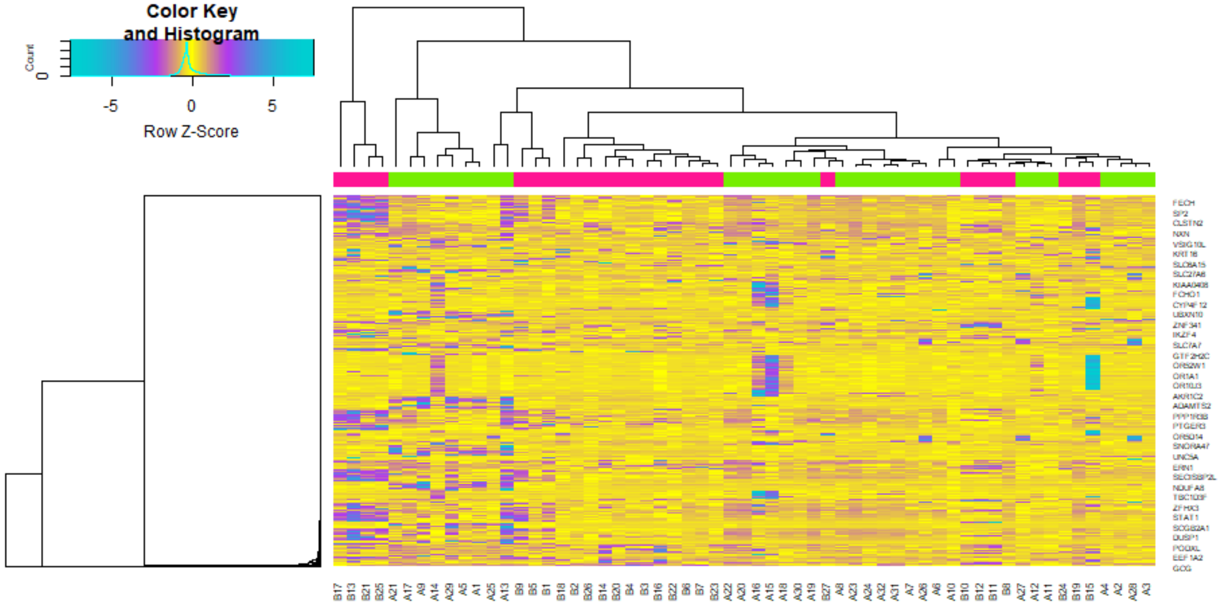

Fig. 2. Heat map of differentially expressed genes. Legend on the top left indicate log fold change of genes. (A1 – A32= normal control samples; B1 – B27 = T1DM samples)

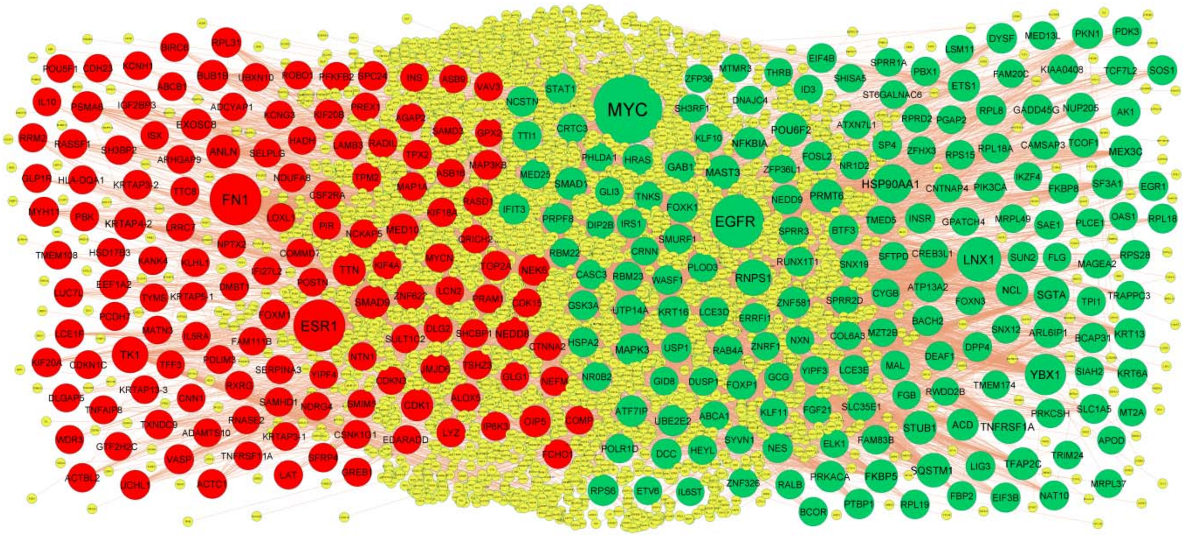

Fig. 3. PPI network of DEGs. The PPI network of DEGs was constructed using Cytoscap. Up regulated genes are marked in green; down regulated genes are marked in red

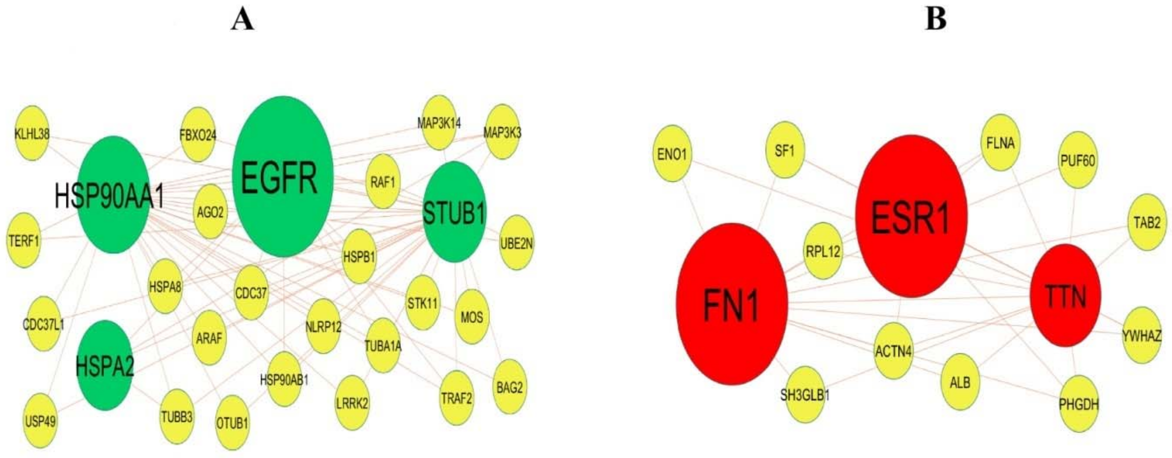

Fig. 4. Modules of isolated form PPI of DEGs. (A) The most significant module was obtained from PPI network with 28 nodes and 63 edges for up regulated genes (B) The most significant module was obtained from PPI network with 14 nodes and 30 edges for down regulated genes. Up regulated genes are marked in green; down regulated genes are marked in red.

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

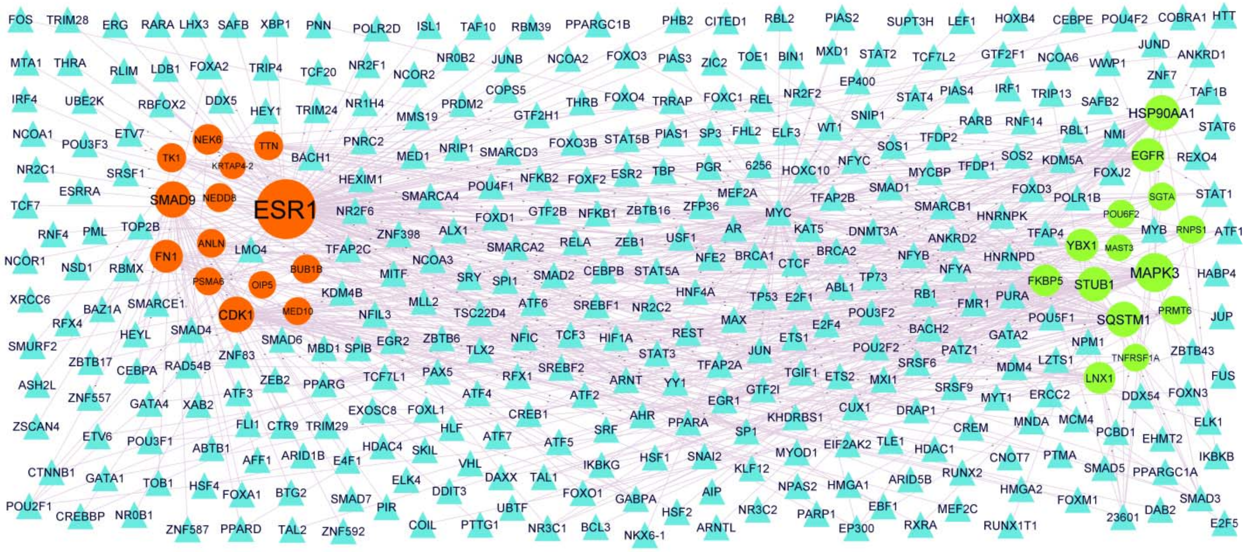

Fig. 6. TF - hub gene regulatory network. The blue color triangle nodes represent the key TFs; up regulated genes are marked in green; down regulated genes are marked in red.

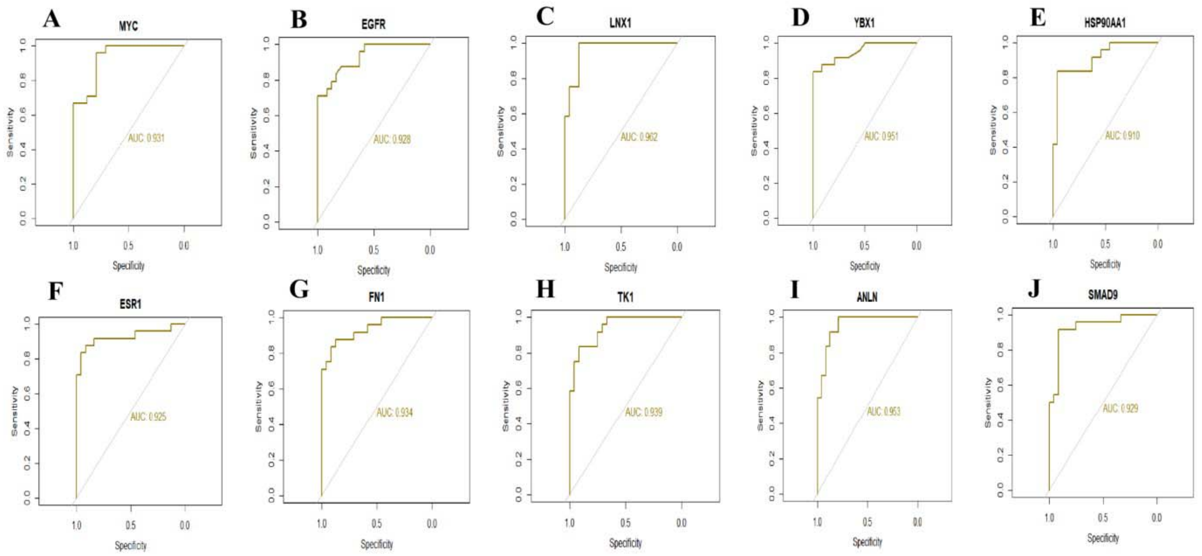

Fig. 7 ROC curve validated the sensitivity, specificity of hub genes as a predictive biomarker for dementia prognosis. A) MYC B) EGFR C) LNX1 D) YBX1 E) HSP90AA1 F) ESR1 G) FN1 H) TK1 I) ANLN J) SMAD9

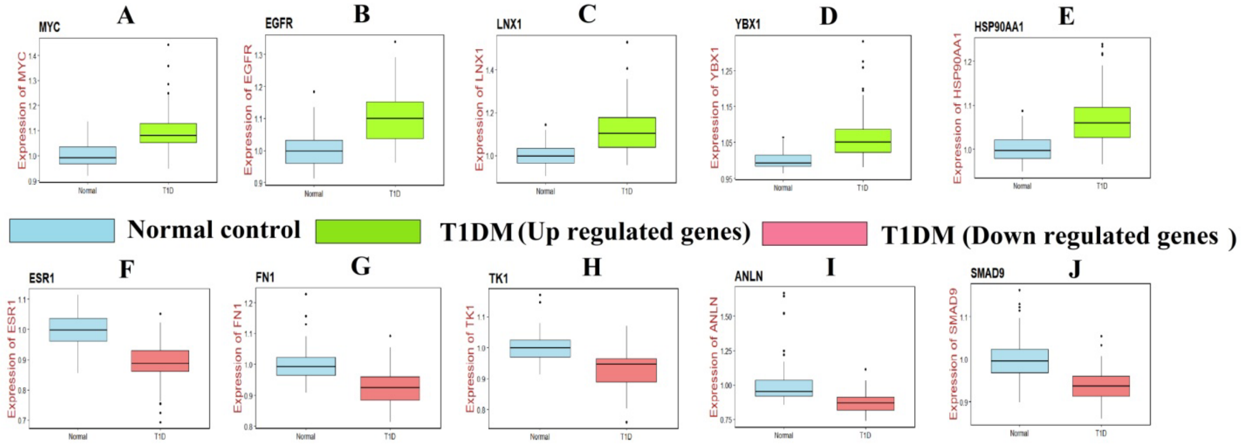

Fig. 8 Validation of hub genes by RT- PCR. A) MYC B) EGFR C) LNX1 D) YBX1 E) HSP90AA1 F) ESR1 G) FN1 H) TK1 I) ANLN J) SMAD9