

Bioinformatics analysis of myocardial immune progression

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ABSTRACT

The immune infiltration and molecular mechanisms underlying septic cardiomyopathy (SC) have not been completely elucidated. This study aimed to identify key genes related to SC and elucidate the potential molecular mechanisms. The weighted correlation network analysis (WGCNA), linear models for microarray analysis (LIMMA), protein-protein interaction (PPI) network, CIBERSORT, Kyoto Encyclopedia of Genes and Genomes pathway (KEGG), and gene set enrichment analysis (GSEA) were applied to assess the key pathway and hub genes involved in SC. We identified 10 hub genes, namely, LRG1, LCN2, PTX3, E LANE, TCN1, CLEC4D, FPR2, MCEMP1, CEACAM8, and CD177. Furthermore, we used GSEA for all genes and online tools to explore the function of the hub genes. Finally, we took the intersection between differential expression genes (DEGs) and hub genes to identify LCN2 and PTX3 as key genes. We found that immune-related pathways played vital roles in SC. LCN2 and PTX3 were key genes in SC progression, which mainly showed an anti-inflammatory effect. The significant immune cells in cardiomyocytes of SC were neutrophils and M2 macrophages. These cells may have the potential to be prognostic and therapeutic targets in the clinical management of SC. Excessive anti-inflammatory function and neutrophil infiltration are probably the primary causes of SC.

Keywords: septic cardiomyopathy; immune infiltration; gene set enrichment analysis (GSEA); weighted correlation network analysis (WGCNA).

1. Introduction

Researchers recognize sepsis as a life-threatening condition that is caused by a dysregulated host response to infection [1]. It is the immune response of the organism to pathogens and immunogenic substances, causing autoimmune damage. Sepsis is common in severe health conditions, and the development of sepsis may lead to septic shock and multiple organ dysfunction syndromes. The heart is the main target organ of sepsis, and more than 50% of patients with severe sepsis have myocardial dysfunction, which is called septic cardiomyopathy (SC) [2]. However, due to a lack of uniform diagnostic criteria, the prevalence of SC varies in different reports. Beesley et al. reported the incidence of myocardial dysfunction in sepsis patients as ranging from 10% to 70% [3].

Inflammatory responses and immune cell infiltration widely exist in many types of cardiomyopathy. For example, in heart tissue with diabetic cardiomyopathy, inflammatory responses have been found to be significantly activated, as manifested by infiltration of multiple immune cells, increased cytokines, and multiple chemical factors [4]. Similar results have also been confirmed in animal models [5, 6]. In the state of diabetes mellitus, macrophages may induce tissue infiltration, transform into the proinflammatory phenotype of M1, and be associated with the activation of inflammatory signaling pathways in leukocytes [7]. Thus, inflammatory responses are closely related to cardiac function. Myocardial dysfunction can increase sepsis-induced mortality, but no reports have elucidated the underlying pathophysiological mechanisms of SC. The molecular mechanism that may be involved in the pathogenesis of SC remains to be studied, and there is a need to screen potential targets for the treatment of SC. Among the pathogenic factors contributing to SC, the imbalanced inflammatory responses caused by sepsis directly correlate with the dysfunction of myocardial cells. Previous studies have reported that sepsis begins with the host immune system's response to invasive pathogens, eventually leading to activation of the innate immune response [8]. Bacterial products, including endotoxins and exotoxins, can directly or indirectly stimulate various target cells, including monocytes, polymorphonuclear neutrophils, or endothelial cells, thereby causing inflammation [9]. Endotoxins and exotoxins, through varied signal transduction pathways, activate both positive and negative feedback loops within the immune system. Sepsis-induced dysregulation of the normal immune response can lead to a variety of harmful effects, including SC. Therefore, a thorough understanding of the molecular immune mechanism involved in the pathogenesis of SC could be one of the breakthroughs that may help in the treatment of SC in the future.

In this study, we downloaded the gene expression profile (GSE79962) deposited by Matkovich et al. from Gene Expression Omnibus (GEO) databases to uncover further the biomarkers associated with SC development and progression [10]. We aimed to identify key genes related to SC, as well as to further elucidate the potential molecular mechanisms through bioinformatics analysis.

2. Materials and Methods

2.1 Data

We downloaded microarray data GSE79962 from the NCBI Gene Expression Omnibus database (GEO, <http://www.ncbi.nlm.nih.gov/geo/>). The data involved ischemic heart disease (IHD, 11 samples), non-failing heart (control, 11 samples), dilated cardiomyopathy (DCM, 9 samples), and septic cardiomyopathy (SC, 20 samples). We chose all the samples in the study. We downloaded the annotation information of the microarray, GPL6244, Affymetrix Human Gene 1.0 ST Array [transcript (gene) version]. We preprocessed the raw data using R version 3.6.0. The analysis workflow is presented in **Fig. 1**.

2.2 WGCNA network construction

We constructed co-expression networks using the weighted correlation network analysis (WGCNA) package in R [11]. We did not filter genes. We imported gene expression values into WGCNA to create co-expression modules using the automatic network construction function `blockwiseModules` with default settings. We set the power value by the condition of scale independence as 0.9. The unsigned TOMType `mergeCutHeight` was 0.25, and the `minModuleSize` was 50.

2.3 Module and gene selection

To find biologically or clinically significant modules for SC, module eigengenes were used to calculate the correlation coefficient with samples. We calculated the intramodular connectivity (function `softConnectivity`) of each gene. We thought genes with high connectivity tended to be hub genes which might have essential functions. We imported the positive correlation modules into Cytoscape software (version 3.7.1), using the MCODE plugin, setting the degree cut-off at no less than 10, to screen the key sub-modules.

2.4 Functional analysis of module genes

Because the three modules were all positively correlated to SC, we imported all genes from these three sub-modules into the STRING database (version 11.0) (<https://string-db.org/>). We obtained the results of gene ontology (GO) enrichment analysis, Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis, and protein-protein interaction (PPI). Significantly enriched GO terms and pathways in genes in a module compared to the background were defined by hypergeometric tests and a threshold of a minimum required interaction score 0.700 (high confi-

dence). After that, we imported a PPI network into Cytoscape software (version 3.7.1), using the cytoHubba plugin to screen the hub genes by 12 methods. We performed functional analysis and disease prediction of hub genes through the online tools Metascape database (<http://metascape.org/>) and ToppGene database (<https://toppgene.cchmc.org/>). We used the “limma” package of the R language to identify the differential expression genes (DEGs) between the SC and control groups, according the $\text{adj.P.Val} < 0.05$ and $|\log\text{FC}| > 0.7$. We screened the shared genes between DEGs and hub genes as key genes.

2.5 GSEA and immune infiltration analysis using the CIBERSORT method

Meanwhile, we performed the gene set enrichment analysis (GSEA) with hallmark gene sets using the 11 control samples and 20 SC samples according to the default values. The criteria of significant results were set as normal enrichment score ($|\text{NES}| > 1$), normal p-value < 0.05 , and FDR < 0.25 . To characterize the immune cell subtypes in SC progression, we applied the CIBERSORT estimate software (<https://cibersort.stanford.edu/>) to quantify the immune cell fractions for the gene expression matrix derived from SC samples. Then, we identified the correlation between the hub genes and immune cell subtypes.

3. Results

3.1 Screening the key modules in the network

Expression data of 18,818 genes in the 51 samples were screened. These samples included SCD, control (non-failing donor heart), ischemic heart disease (IHD), and dilated cardiomyopathy (DCM). They were used to construct the co-expression modules with the WGCNA algorithm. Following the data preprocessing, we set the power value. The power value was four when the condition of scale independence was 0.9 (**Fig. A.1**). We clustered genes into 26 correlated modules. We tried to identify sample-associated co-expression modules using WGCNA (**Fig. 2.A and B**). At last, we got 18 co-expression modules, which were illustrated in the branches of a dendrogram with different colors. We focused just on the SC group. Therefore, we chose the dark green module (Pearson $\text{cor} = 0.69$, $p = 3e-8$), blue module (Pearson $\text{cor} = 0.83$, $p = 3e-14$), and orange module (Pearson $\text{cor} = 0.74$, $p = 4e-10$), as moderately or more positively related with SC. The number of genes in the three modules was 2652 (blue), 73 (dark green), and 2041 (orange). The information about the genes in the three modules is listed in **Table A.1**. The relationship of module membership to gene significance in the modules showed was $\text{cor} = 0.9$ and $p < 1e-200$ in the blue module (**Fig. 2.C**), $\text{cor} = 0.9$ and $p = 3.3e-34$ in the dark green module (**Fig. 2.D**), and $\text{cor} = 0.79$ and $p < 1e-200$ in the orange module (**Fig. 2.E**). We imported the three modules into the Cytoscape software and used the MCODE to screen the three sub-modules, setting the criteria of the MCODE score to more than 10. After screening, we got 58 genes from the orange module (average MCODE score = 33.98), 37 genes from the blue module (average MCODE score = 14.23), and 53 genes from the dark green module (average MCODE score = 41.16) (**Table A.2**).

3.2 Functional enrichment analysis of genes in critical modules

We imported all of the screened genes (a total of 148 genes) from the three modules into the STRING database to construct a PPI network. Meanwhile, we got GO enrichment analysis results according to a false discovery rate (FDR) < 0.05 .

We obtained the top 10 biological process (BP) terms, including neutrophil activation (FDR = 1.29E-22), neutrophil degranulation (FDR = 2.65E-22), regulated exocytosis (FDR = 6.34E-22), exocytosis (FDR = 2.02E-21), leukocyte mediated immunity (FDR = 2.20E-21), leukocyte activation involved in immune response (FDR = 9.78E-21), immune response (9.07E-20), leukocyte activation (FDR = 1.86E-18), secretion (FDR = 1.86E-18), and cell activation (FDR = 2.56E-18) (**Fig. 2.F**). We obtained GO terms of the top 10 cellular components (CC), consisting of secretory granule (FDR = 2.49E-19), cytoplasmic vesicle part (FDR = 1.34E-15), cytoplasmic vesicle (FDR = 4.74E-13), vesicle (FDR = 4.74E-13), tertiary granule (FDR = 4.74E-13), specific granule (FDR = 3.63E-11), secretory granule lumen (FDR = 6.73E-11), secretory granule membrane (FDR = 1.42E-10), ficolin-1 rich granule (FDR = 1.82E-10), and endomembrane system (FDR = 1.33E-09) (**Fig. 3.A**). Meanwhile, we harvested GO terms of 8 molecular functions (MFs), comprising protein binding (FDR = 0.00028), cytokine binding (FDR = 0.00028), enzyme binding (FDR = 0.0018), signaling receptor binding (FDR = 0.0124), CXCR chemokine receptor binding (FDR = 0.0297), protease binding (FDR = 0.0361), cytokine receptor activity (FDR = 0.0361), and pantetheine hydrolase activity (FDR = 0.0361; **Fig. 3.B**). Regarding the KEGG pathway enrichment, the genes were significantly enriched in pathways including neutrophil degranulation (FDR = 4.58E-23), innate immune system (FDR = 1.30E-16), immune system (FDR = 1.30E-16), signaling by interleukins (FDR

= 8.52E-06), cytokine signaling in immune system (FDR = 0.00025), and others (**Fig. 3.C; Table A.3**)

We used Cytoscape software to visualize the PPI network from the STRING database, which is shown in **Fig. 3.D**. Through the cytoHubba plugin, we exported the results of 12 algorithms and screened the top 10 genes as hub genes. These included LRG1, LCN2, PTX3, ELANE, TCN1, FPR2, CLEC4D, MCEMP1, CEACAM8, and CD177 (**Fig. 3.E and Table A.4**).

3.3 GSEA and immunocyte infiltration analysis

The results of GO and KEGG enrichment analysis also indicated that immune and inflammatory events played a vital role in cardiac tissue in SC. Furthermore, the results of GSEA with hallmark gene sets between the control and SC indicated significant differences in the myocardium of SC, such as TGF-beta signaling, TNF-alpha signaling through NF-kappa B, inflammatory response, and TNF and P53 pathways (we set the criteria $|NES| > 1$, $NOM\ p < 0.01$, $FDR\ q < 0.25$; **Fig. 4.A and Table 1**). To characterize the immunocyte status of cardiac tissues in SC, we performed a tissue immune infiltration analysis. We found that there was no significant difference in 22 immune subtypes in the myocardium of SC and the control, except for M2 macrophages (Wilcoxon, $p = 0.032$) and neutrophils (Wilcoxon, $p = 0.00064$; **Fig. 4.C and D**). A heatmap of immune cell subtypes is illustrated in **Fig. 4.B**.

3.4 Identification of the relationship between hub genes and key immune cell subtypes in SC

We found that two subtypes of immune cells in the infiltration were significant. These were neutrophils and M2 macrophages. Importantly, the neutrophils had the highest relative infiltration value. We analyzed the relationship between the 10 hub genes in immune-related pathways and the two immune cell subtypes and found the neutrophils had positive correlations with all hub genes, especially with CLEC4D, CD177, LCN2, and TCN1, but M2 macrophages had negative correlations with all hub genes and neutrophils; **Fig. 4.E**) This suggests that to some extent, neutrophils can promote the progression of SC in the myocardium, but that M2 macrophages do the opposite.

3.5 Investigating the functional role of hub genes and identification of key genes

To further understand how the hub genes were correlated with SC, we applied the Metascape online database to explore their biological functions. The results of the top five GO term enrichments in hub genes included neutrophil degranulation, neutrophil activation involved in immune response, neutrophil activation, neutrophil mediated immunity, and granulocyte activation. The results showed all hub genes are involved in the neutrophil and immune response (**Table 2**). We explored enriched pathways of hub genes involved in neutrophil degranulation, the innate immune system, antimicrobial peptides, and similar topics (**Table A.5**). We also predicted diseases related to hub genes using the ToppGene database. These diseases included sepsis, immune neutropenia, septicemia, and others (**Table 3 and Table A.5**). We found 467 DEGs between the SC group and the control (**Table A.6**). Finally, we took the intersection between DEGs and hub genes to identify LCN2 and PTX3 as key genes (**Fig. 4.F**). As for the key genes, we compared the expression levels of LCN2 and PTX3 in different kinds of myocardial injury from these samples. We found LCN2 and PTX3 had significantly higher expression in the SC group (**Fig. A.2**).

4. Discussion

In this study, we screened key modules in SC by analyzing a public dataset (GSE79962). Compared with the control group, IHD group, and DCM group, a total of three modules were positively correlated with SC. These included the orange module, blue module, and dark green module. We chose 148 genes from the three modules using the MCODE plugin of Cytoscape for functional enrichment analysis. Notably, we found most genes in the three modules were enriched in the immune response, leukocyte activation, neutrophil degranulation, and similar events.

Regarding the KEGG pathway enrichment, the genes were significantly enriched in immune-related pathways, including neutrophil degranulation, the innate immune system, the immune system, and cytokine signaling in the immune system. The results of GSEA with hallmark gene sets between control and SC indicated that significantly different pathways in the myocardium of SC were immune-related. Neutrophils degranulated during phagocytosis, releasing a series of lysosomal enzymes, which caused damage to blood vessels and surrounding tissues, leading to cardiac dysfunction [12]. Sepsis leads to an auto-amplifying cytokine production known as the cytokine storm. At the same time, activation

of Toll-like receptors (TLRs) releases a large number of inflammatory cytokines, such as TNF, IL-1, interferon regulatory factor 3 (IRF3) [13]. The activation of these immune responses leads to damage of myocardial tissue and cardiac dysfunction. Previous studies have reported that TLRs can attenuate SC through activation of innate immune and inflammatory responses [14, 15]. TLR is a kind of pattern recognition receptor that can activate the innate immunity response, playing a critical role through activation of NF κ B which is an important transcription factor controlling the expression of inflammatory cytokine genes [16]. TLRs play a major role in the pathophysiology of cardiac dysfunction during sepsis [14]. In an animal model, TLR2 was found that can influence cardiac function through deteriorating sarcomere shortening [17, 18]. TLRs deficiency attenuated cardiac dysfunction in a mouse model through inhibition of sepsis-induced activation of TLR4 mediated NF- κ B signaling pathways, and prevention of the macrophage and neutrophil infiltration. In addition, lipopolysaccharide (LPS) has been demonstrated to induced macrophage inflammation through TLRs, leading to the release of proinflammatory cytokines [19]. In patients with sepsis, increased serum lactate levels increased mortality through activation of innate immune and inflammatory responses [20, 21]. Through the CIBERSORT method, we found that the infiltration value of neutrophils and M2 macrophages in the myocardium of SC is significant. Therefore, we found that immunity and inflammation play important roles in myocardial dysfunction in SC. In this condition, neutrophils were positively correlated with immune-related genes, and M2 macrophages were negatively correlated with immune-related genes.

Macrophages are the “frontier soldiers” of innate immunity. The function of macrophages is classified into two types, type M1 (classically activated) and type M2 (alternatively activated). Type M1 macrophages can secrete chemokines for a proinflammatory function, and type M2 macrophages mainly secrete chemokines in the late stage of inflammation to play an anti-inflammatory role [22, 23]. M2 macrophages mainly promote tissue remodeling and repair, and previous studies showed that an increase in M2 macrophage infiltration in myocardium promotes fibrosis [23-25]. The decrease of M2 macrophages in SC leads to a reduction of anti-inflammatory chemokines and supports the progression of SC. The polarization of the M1 macrophage is mainly regulated by transcription factors IRF5 and STAT1, and the M2 macrophage is regulated by IRF4 and STAT6 [26]. Many immunomodulators can promote M1 macrophage polarization, such as IFN, TNF, IL-1, IL-6, LPS, B-cell activator (BAFF), and proliferation-inducing ligand (APRIL) [26-29]. In addition, some metabolites, such as saturated fatty acids and oxidized lipoproteins, can also induce M1 macrophage polarization [27]. Similarly, inflammatory factors, such as IL-4, IL-13, IL-10, IL-33 and TGF β , as well as metabolites such as unsaturated fatty acids and retinoic acid, can induce M2 macrophage polarization [30, 31]. Likewise, neutrophils are key factors in the immune response to sepsis. Under normal conditions, neutrophils control infection, but excessive stimulation or dysregulated neutrophil functions are believed to be responsible for sepsis pathogenesis [12]. In SC, we found significant neutrophil infiltration in cardiac tissues.

We screened 10 hub genes from the PPI network constructed from 148 genes. These 10 genes are also involved in several immune-related pathways directly, which include LRG1, LCN2, PTX3, ELANE, TCN1, CLEC4D, FPR2, MCEMP1, CEACAM8, and CD177. Next, we used online tools (the ToppGene and Metascape databases) to explore the function of the hub genes. The results showed that the hub genes were related to immune-related pathways and diseases. Among these genes, LRG1 is highly correlated with neutrophils and other genes composed of TCN1, FPR2, CLEC4D, and CD177. LRG1 is expressed during granulocyte differentiation. From the GeneCards database (<https://www.genecards.org/>), we found that the super pathway for LRG1 is the innate immune system. BP terms included response to bacterium, positive regulation of transforming growth factor-beta receptor signaling pathway, neutrophil degranulation, and similar terms. Recombinant human LRG is used as a diagnostic aid in acute appendicitis [32]. Similarly, LRG1 may be used as a diagnostic marker for SC.

In our research, we found that LCN2 and PTX3 in 10 hub genes existed in DEGs, as key genes. LCN2, encoding the lipocalin-2 (also known as neutrophil gelatinase-associated lipocalin), is a critical iron regulatory protein during physiological and inflammatory conditions and exerts mostly a protective role in inflammatory bowel diseases and urinary tract infection by limiting bacterial growth [33, 34]. In the heart, some reports also indicated that LCN2 was significantly expressed during *in vivo* and *in vitro* experiments on cardiac hypertrophy and heart failure, and high plasma LCN2 was correlated with high mortality and myocardial dysfunction in severe sepsis [35, 36]. Nevertheless, Guo et al. found that LCN2 $^{-/-}$ mice displayed an up-regulation of M1 macrophages but down-regulation of M2 macrophages. These mice had profound up-regulation of proinflammatory cytokines, suggesting that LCN2 plays a role as an anti-inflammatory regulator in macrophage activation [37]. Overexpression of LCN2 is consistent with down-regulation of M2 macrophages in SC. PTX3 plays a role in the regulation of innate resistance to pathogens and inflammatory reactions. Paeschke et al. showed that inflammatory injury of heart tissue was aggravated in mice when PTX3 was knocked down [38]. Yamazaki et al. demonstrated that bacterial LPS, induced expression of anti-microbial glycoproteins-PTX3 and LCN2 in macrophages [39]. Therefore, we concluded that LCN2 and PTX3 might lead to excessive anti-inflammatory effects for SC progression.

5. Conclusion

To sum up, we found that genes in three modules played vital roles in the immune-related pathways. LCN2 and PTX3 were key genes in SC progression and mainly showed anti-inflammatory effects. The significant immune cells in cardiomyocytes of SC were neutrophils and M2 macrophages. Therefore, LCN2 and PTX3 may have the potential to perform as prognostic and therapeutic targets in the clinical management of SC. Excessive anti-inflammatory function and neutrophil infiltration were probably the primary causes of SC, but this needs further analysis.

Data availability:

Applicable. The data files with the raw materials from the RNA array can be downloaded from the data repository at GEO accession number: GSE79962.

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Table 1: The top five pathways enriched by all genes through GSEA ($|NES| > 1$, Nom $p < 0.01$, and FDR $q < 0.25$), GSEA (gene set enrichment analysis)

Name	NES	Nom p-value	FDR q-val
HALLMARK_TGF_BETA_SIGNALING	-1.76045	0.00998	0.18903
HALLMARK_TNFA_SIGNALING_VIA_NFKB	-1.65812	0.001961	0.242987
HALLMARK_P53_PATHWAY	-1.63801	0.005725	0.19739328
HALLMARK_IL2_STAT5_SIGNALING	-1.5659359	0.003937008	0.1933887
HALLMARK_ESTROGEN_RESPONSE_LATE	-1.4913071	0.007797271	0.18019646

Table 2: The top five GO items enriched by hub genes, GO (gene ontology)

Category	Name	q-value	Enriched Genes
GO: BP	neutrophil degranulation	9.59752E-05	CD177,CEACAM8,CLEC4D,ELANE,FPR2,LCN2,LRG1,MCEMP1,PTX3,TCN1
GO: BP	neutrophil activation involved in immune response	9.59752E-05	CD177,CEACAM8,CLEC4D,ELANE,FPR2,LCN2,LRG1,MCEMP1,PTX3,TCN1
GO: BP	neutrophil activation	9.59752E-05	CD177,CEACAM8,CLEC4D,ELANE,FPR2,LCN2,LRG1,MCEMP1,PTX3,TCN1
GO: BP	neutrophil mediated immunity	9.59752E-05	CD177,CEACAM8,CLEC4D,ELANE,FPR2,LCN2,LRG1,MCEMP1,PTX3,TCN1
GO: BP	granulocyte activation	9.59752E-05	CD177,CEACAM8,CLEC4D,ELANE,FPR2,LCN2,LRG1,MCEMP1,PTX3,TCN1

Table 3: The top five diseases enriched by hub genes

ID	Name	p-value	FDR	Enriched Genes
C0243026	Sepsis	1.73E-07	7.56E-05	FPR2,CLEC4D,CD177,ELANE,LCN2,PTX3
C0272175	Immune neutropenia	2.04E-06	4.45E-04	CD177,ELANE
C0036690	Septicemia	3.99E-06	5.81E-04	FPR2,CD177,ELANE,LCN2,PTX3
C0085578	Thalassemia Minor	3.08E-05	3.36E-03	CD177,LCN2
C0005283	beta Thalassemia	4.51E-05	3.74E-03	CD177,ELANE,LCN2

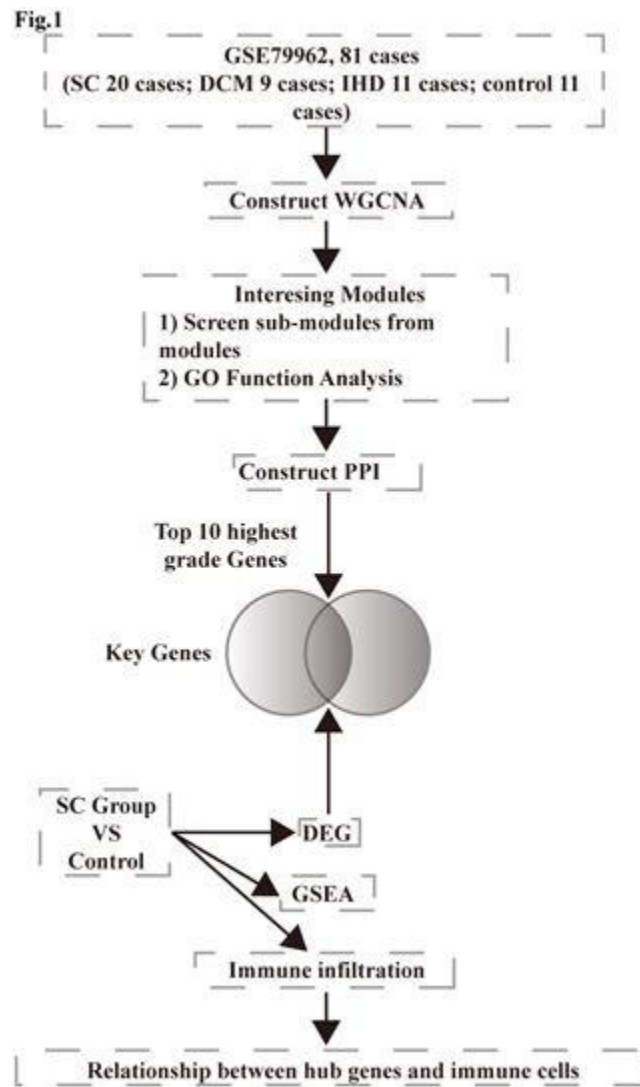


Figure 1:Workflow used for bioinformatics analyses.

Fig.S1

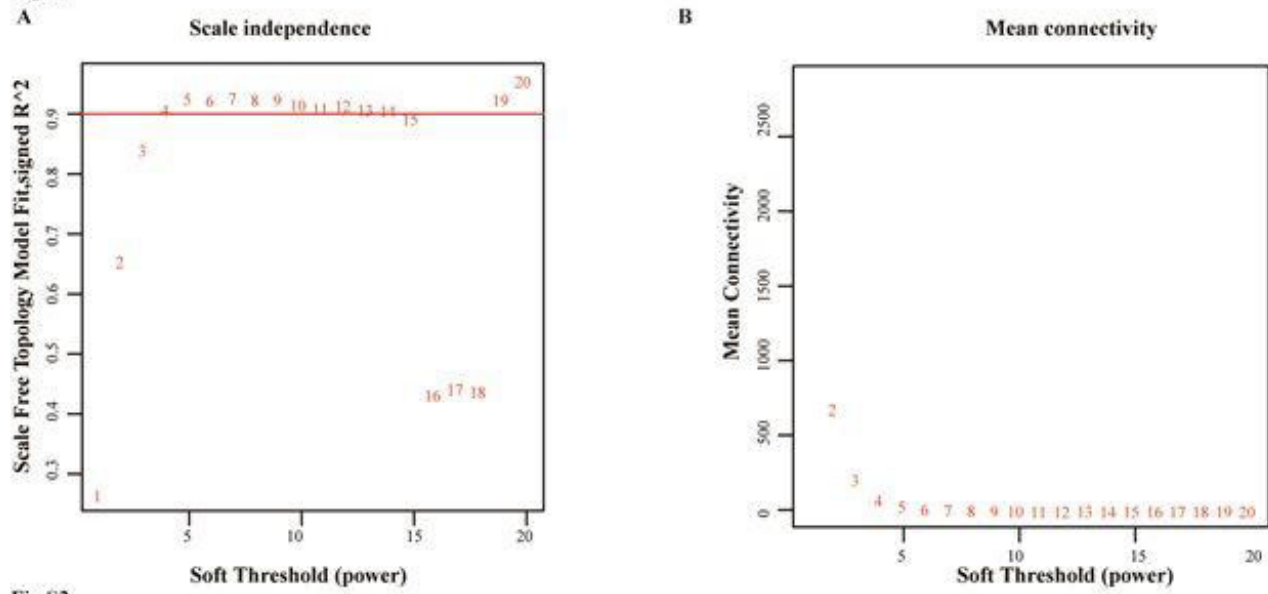


Fig.S2

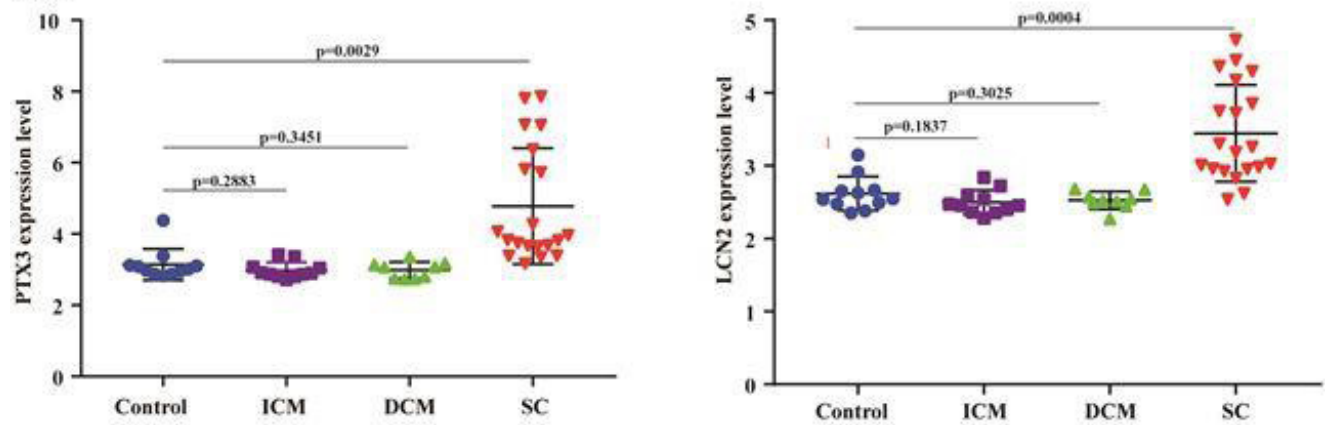


Figure S1-2

Fig.2

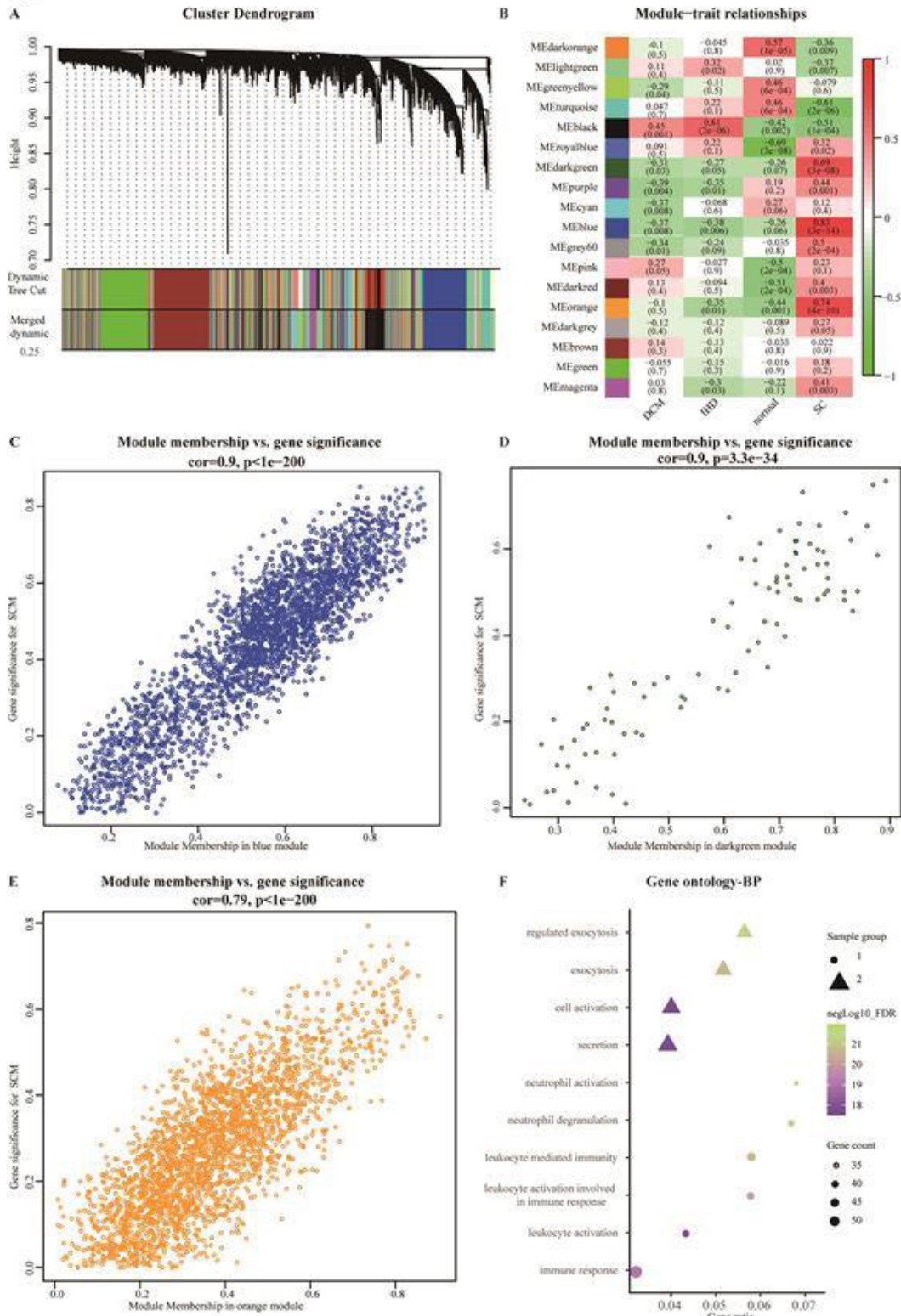


Figure 2: Overview of WGCNA network construction of all genes (A) Gene modules' dendrogram plots of all genes; (B) module-trait relationships of four groups in 18 modules. (C-E) Module membership vs. gene significance between three significant modules, including blue module (Pearson $cor = 0.9, p < 1e-200$), dark green module ($cor = 0.9, p = 3.3e-34$), and orange module (Pearson $cor = 0.79, p < 1e-200$); F) The bubble diagram showing the GO (biological process, BP) function enrichment of genes in sub-modules. The size represents the gene counts, and node colors show the gene expression negative Log_{10_FDR} (false discovery rate).

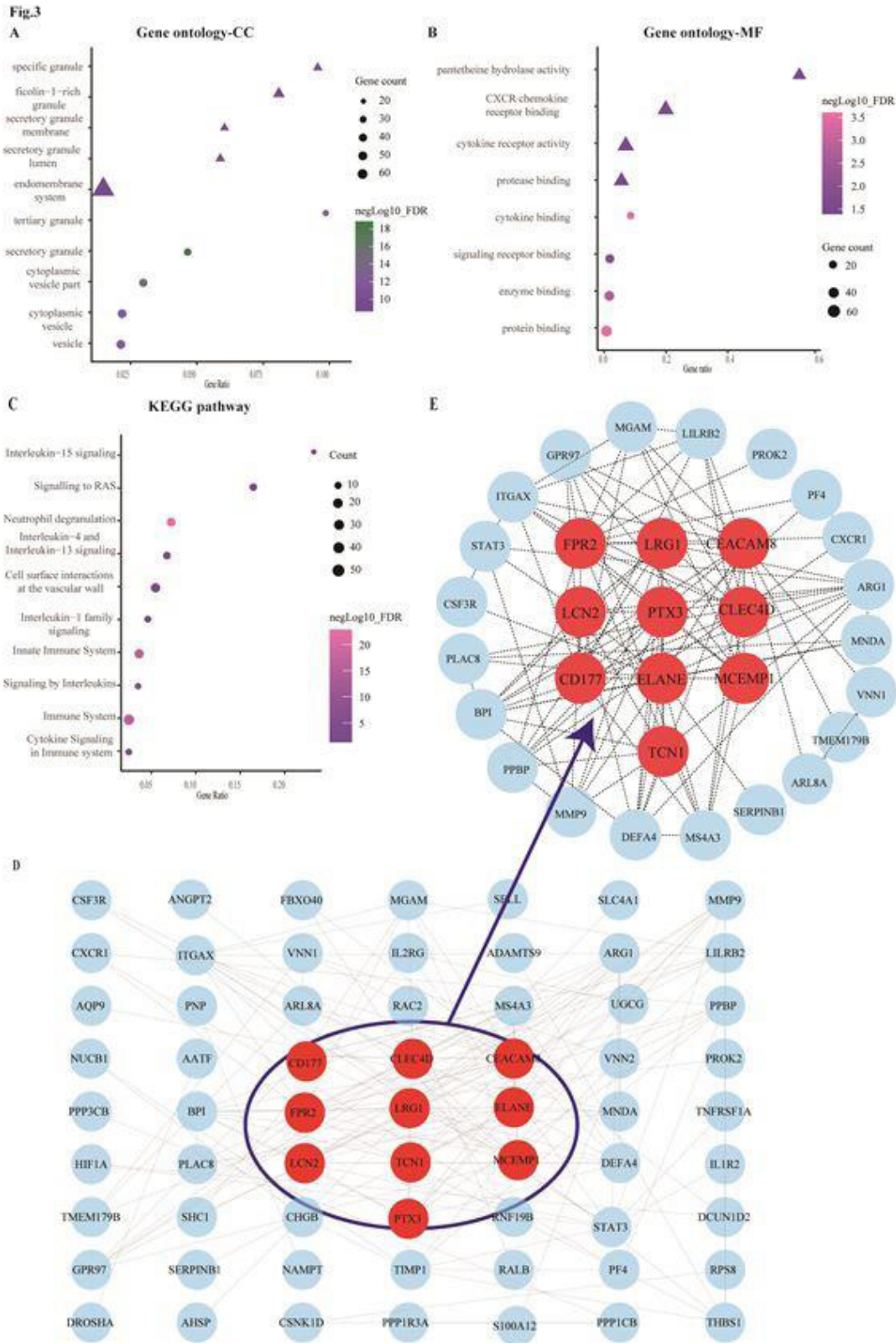


Figure 3: Analysis of GO function, KEGG pathways, and PPI network of genes in sub-modules. (A-C) The bubble map showing the GO function (cellular component, CC, and molecular function, MF) and KEGG pathways were constructed by the STRING database. The sizes represent negative Log₁₀ (FDR). (D) The gene PPI network was also constructed based on the STRING database. (E) The plots showing the top 10 higher degree hub genes for SC.

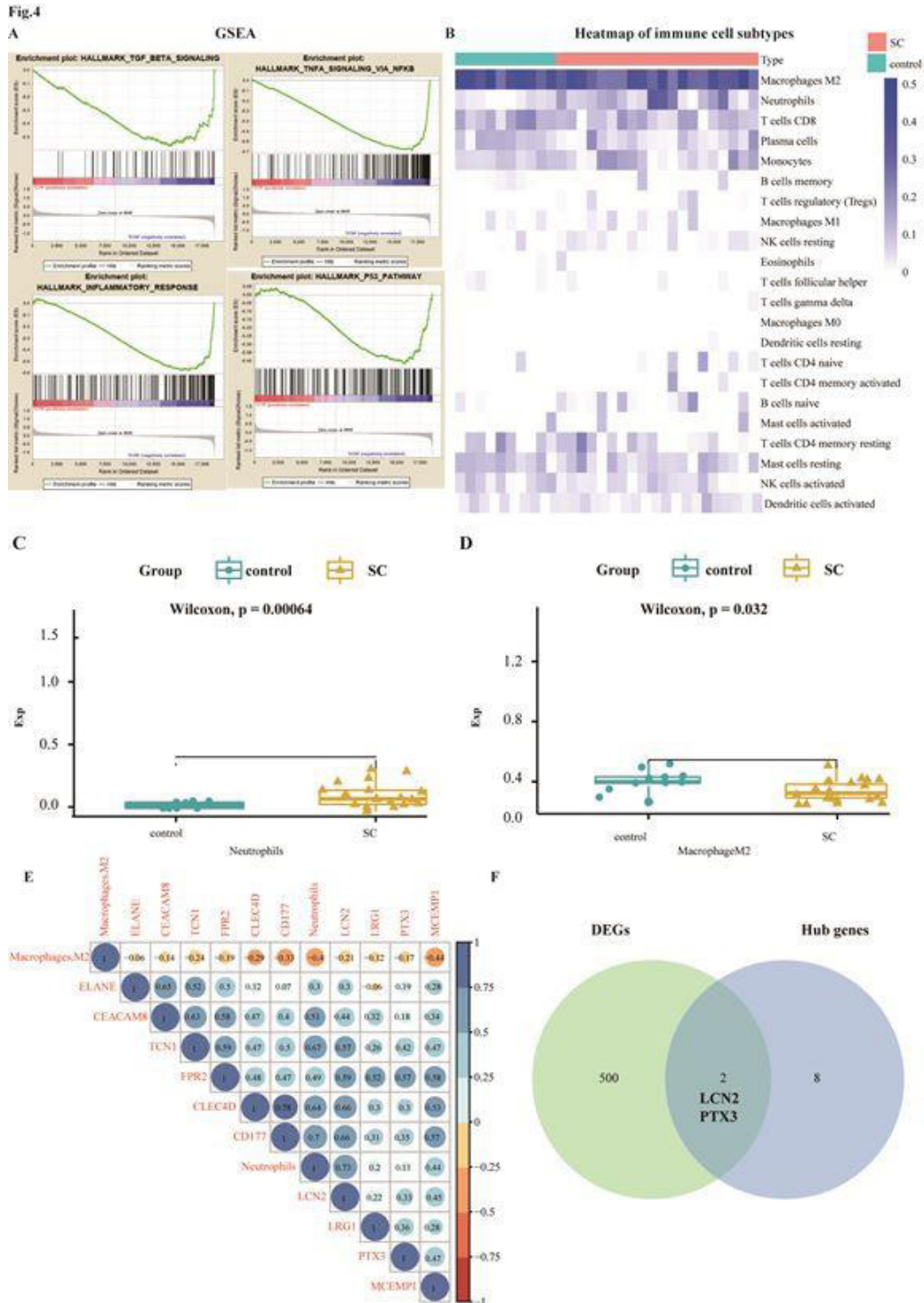


Figure 4: Immunocyte infiltration analysis and potential immunocyte subtype detection. (A) This diagram shows the immune-related pathways by GSEA analysis. (B) This heatmap shows the immunocyte infiltration difference between SC and control heart samples. (C, D) Box plots presenting significantly infiltrated immunocyte subtypes, neutrophils, and M2 macrophages. (E) This correlated heatmap shows the relationship between immunocytes and hub genes. (F) Intersection between DEGs and hub genes, identifying the key genes, LCN2 and PTX3.

Table A.1. The information about the genes in the three modules.

Table A.1 Genes in darkgreen module	
Name	Node
WDR63	darkgreen
VNN2	darkgreen
VNN1	darkgreen
VAV1	darkgreen
TNFSF13B	darkgreen
TCN1	darkgreen
SMPD4	darkgreen
SLC4A1	darkgreen
SIRPB1	darkgreen
SELL	darkgreen
S100A12	darkgreen
ROPN1L	darkgreen
RIPOR2	darkgreen
RAC2	darkgreen
PROK2	darkgreen
PPBP	darkgreen
POMC	darkgreen
PLAC8	darkgreen
PI3	darkgreen
PF4	darkgreen
PADI2	darkgreen
NFE2	darkgreen
MYO1G	darkgreen
MYO1F	darkgreen
MXD1	darkgreen
MS4A3	darkgreen
MNDA	darkgreen
MMP9	darkgreen
MIR129-2	darkgreen
MGAM	darkgreen
MEFV	darkgreen
MCEMP1	darkgreen
LRG1	darkgreen
LILRB2	darkgreen
LCN2	darkgreen
ITGAX	darkgreen
IL5RA	darkgreen
IL2RG	darkgreen
IL1RN	darkgreen
IL1R2	darkgreen

IL18RAP	darkgreen
HSPA6	darkgreen
HEMGN	darkgreen
HAVCR2	darkgreen
HACD1	darkgreen
GYPA	darkgreen
FREM3	darkgreen
FPR2	darkgreen
FCN1	darkgreen
FAM172A	darkgreen
ELMOD1	darkgreen
ELANE	darkgreen
DZANK1	darkgreen
DROSHA	darkgreen
DEFA4	darkgreen
CYTIP	darkgreen
CXCR2	darkgreen
CXCR1	darkgreen
CST7	darkgreen
CSF3R	darkgreen
CR1	darkgreen
CLEC4D	darkgreen
CHGB	darkgreen
CEACAM8	darkgreen
CD177	darkgreen
CCNYL2	darkgreen
C14orf177	darkgreen
BPI	darkgreen
BCL2A1	darkgreen
ARG1	darkgreen
AQP9	darkgreen
AHSP	darkgreen
ADGRG3	darkgreen

Table A.2 Genes from the three modules (average MCODE score ≥ 10)

Table A.2 Genes from the darkgreen module (average MCODE score = 41.46)	
name	MCODE_Score
SLC4A1	38.95243902
SELL	41.67536232
RIPOR2	40.95459579
RAC2	41.67536232
PROK2	41.67536232
PPBP	41.67536232
PLAC8	41.67536232
PF4	41.91120507
NFE2	41.67536232
MYO1G	41.67536232
MYO1F	41.67536232
MXD1	41.67536232
MS4A3	41.67536232
MNDA	41.67536232
MMP9	41.67536232
MIR129-2	38.8641115
MGAM	41.67536232
MCEMP1	41.67536232
LRG1	41.67536232
LILRB2	41.67536232
LCN2	41.67536232
ITGAX	40.95459579
IL2RG	41.67536232
IL1R2	41.67536232
HSPA6	41.91120507
HEMGN	41.67536232
HACD1	41.67536232
FPR2	41.67536232
ELANE	41.78787879
DROSHA	41.67536232
CYTIP	41.91120507
ELMOD1	40
CST7	41.67536232
CSF3R	41.67536232
DEFA4	38.90487805
CLEC4D	40.62727273
CHGB	41.67536232
CEACAM8	40.82663848
CD177	41.67536232

BPI	41.67536232
BCL2A1	41.67536232
ARG1	41.67536232
AQP9	41.67536232
AHSP	39.95354239
ADGRG3	41.67536232
SIRPB1	37
S100A12	41.67536232
IL18RAP	41.67536232
CXCR1	41.67536232
CR1	41.67536232
VNN2	41.67536232
VNN1	34
TCN1	40.75151515

Table A.3 The results of pathway enrichment

ID	Description	gene count	FDR	gene symbol
HSA-6798695	Neutrophil degranulation	35	4.58E-23	ARG1,ARL8A,BPI,CD177,CD55,CEACAM8,CLEC4D,CR1,CXCR1,DEFA4,ELANE,FPR2,GPR97,HSPA6,ITGAX,LCN2,LILRB2,LRG1,MCEMP1,MGAM,MMP9,MNDA,MS4A3,MVP,PLAC8,PNP,PPBP,PTX3,S100A12,SELL,SERPINB1,SIRPB1,TCN1,TMEM179B,VNN1
HSA-168249	Innate Immune System	39	1.30E-16	ARG1,ARL8A,BPI,CD177,CD55,CEACAM8,CLEC4D,CR1,CXCR1,DEFA4,ELANE,FPR2,GPR97,HSPA6,ITGAX,LCN2,LILRB2,LRG1,MAPKAPK2,MCEMP1,MGAM,MMP9,MNDA,MS4A3,MVP,OTUD5,PLAC8,PNP,PPBP,PPP3CB,PTX3,RIPK2,S100A12,SELL,SERPINB1,SIRPB1,TCN1,TMEM179B,VNN1
HSA-168256	Immune System	52	1.30E-16	ARG1,ARL8A,BPI,CD177,CD55,CEACAM8,CLEC4D,CR1,CSF3R,CXCR1,DEFA4,ELANE,FBXO40,FPR2,GPR97,HIF1A,HSPA6,IFITM2,IL18RAP,IL1R2,IL1RL1,IL2RG,ITGAX,LCN2,LILRB2,LRG1,MAPKAPK2,MCEMP1,MGAM,MMP9,MNDA,MS4A3,MVP,OTUD5,PLAC8,PNP,PPBP,PPP3CB,PTX3,RIPK2,RNF19B,S100A12,SELL,SERPINB1,SHC1,SIRPB1,STAT3,TCN1,TIMP1,TMEM179B,TNFRSF1A,VNN1
HSA-449147	Signaling by Interleukins	16	8.52E-06	CSF3R,HIF1A,IL18RAP,IL1R2,IL1RL1,IL2RG,ITGAX,LCN2,MAPKAPK2,MMP9,RIPK2,S100A12,SHC1,STAT3,TIMP1,TNFRSF1A
HSA-1280215	Cytokine Signaling in Immune system	17	0.00025	CSF3R,HIF1A,IFITM2,IL18RAP,IL1R2,IL1RL1,IL2RG,ITGAX,LCN2,MAPKAPK2,MMP9,RIPK2,S100A12,SHC1,STAT3,TIMP1,TNFRSF1A
HSA-6785807	Interleukin-4 and Interleukin-13 signaling	7	0.00087	HIF1A,IL2RG,ITGAX,LCN2,MMP9,STAT3,TIMP1
HSA-202733	Cell surface interactions at the vascular wall	7	0.0033	ANGPT2,CD177,CEACAM8,ITGAX,PF4,SELL,SHC1
HSA-8983432	Interleukin-15 signaling	3	0.0088	IL2RG,SHC1,STAT3
HSA-167044	Signalling to RAS	3	0.0166	MAPKAPK2,RALB,SHC1
HSA-446652	Interleukin-1 family signaling	6	0.0166	IL18RAP,IL1R2,IL1RL1,RIPK2,S100A12,STAT3
HSA-6783783	Interleukin-10 signaling	4	0.0166	IL1R2,STAT3,TIMP1,TNFRSF1A
HSA-109582	Hemostasis	12	0.0346	ANGPT2,CD177,CEACAM8,ITGAX,NFE2,PF4,PPBP,RAC2,SELL,SHC1,THBS1,TIMP1
HSA-400253	Circadian Clock	4	0.0435	CSNK1D,HIF1A,NAMPT,PPP1CB

Table A.4 Hub genes

node_name	MCC	DMNC	MNC	Degree	EPC	Bottle Neck	EcCentricity	Closeness	Radiality	Between-ness	Stress	Clustering Coefficient
CEACAM8	5778	0.51222	12	15	18.529	12	0.13228	28.28333	5.47457	480.8826	1058	0.3619
FPR2	5767	0.71599	9	13	17.658	6	0.13228	26.61667	5.39359	320.0572	748	0.42308
CD177	5760	0.71599	9	9	16.864	1	0.13228	23.28333	5.16683	8.68636	54	0.83333
CLEC4D	5760	0.71599	9	9	16.387	2	0.13228	23.28333	5.16683	8.68636	54	0.83333
MCEMP1	5760	0.71599	9	9	16.421	1	0.13228	23.28333	5.16683	8.68636	54	0.83333
ELANE	5198	0.49759	12	14	18.339	4	0.13228	28.11667	5.52316	373.0438	1058	0.37363
LRG1	5184	0.66826	9	9	17.026	1	0.13228	23.78333	5.24781	23.50211	184	0.77778
PTX3	5184	0.66826	9	9	17.223	1	0.13228	23.78333	5.24781	23.50211	184	0.77778
TCN1	5184	0.66826	9	9	17.08	1	0.13228	23.78333	5.24781	23.50211	184	0.77778
LCN2	5164	0.64439	9	9	17.568	1	0.15873	24.28333	5.345	56.7632	230	0.75
BPI	5070	0.55867	10	10	17.752	2	0.13228	25.28333	5.345	80.42913	328	0.62222
ARG1	5066	0.53872	10	10	17.737	9	0.15873	24.86667	5.36119	187.8673	454	0.6
DEFA4	5052	0.59666	9	9	17.727	1	0.13228	24.36667	5.28021	44.10924	216	0.69444
ITGAX	5042	0.76834	7	9	16.07	13	0.15873	25.28333	5.42598	371.1429	714	0.58333
MGAM	5040	0.76834	7	7	15.433	1	0.13228	22.28333	5.13443	0	0	1
LILRB2	5040	0.76834	7	7	15.64	1	0.13228	22.28333	5.13443	0	0	1
MS4A3	726	0.52483	8	8	16.584	2	0.11338	23.74286	5.16683	55.04209	216	0.64286
GPR97	720	0.71324	6	6	14.732	1	0.11338	20.90952	4.94007	0	0	1
MMP9	156	0.3791	10	10	16.676	1	0.15873	26.03333	5.49077	260.0984	742	0.42222
PPBP	42	0.33413	9	9	15.604	2	0.13228	24.98333	5.345	183.7392	688	0.38889
MNDA	26	0.56839	4	6	12.257	4	0.13228	21.28333	5.05345	213.803	458	0.4
PLAC8	24	0.56839	4	4	11.75	1	0.13228	19.95	4.98866	0	0	1
TIMP1	16	0.38896	5	7	11.509	7	0.15873	22.9	5.23162	263.3214	598	0.33333
THBS1	14	0.47366	4	6	10.153	3	0.13228	20.98333	5.02106	192.3274	454	0.33333
STAT3	13	0.25931	5	10	14.476	21	0.19841	26.83333	5.58795	847.6075	1656	0.08889
PF4	12	0.38896	5	5	11.263	7	0.13228	21.68333	5.11824	74.7	200	0.6
VNN1	7	0.46346	3	4	7.933	3	0.11338	19.54286	4.82669	66.0303	80	0.5
ARL8A	6	0.46346	3	3	7.441	1	0.11338	18.62619	4.7619	0	0	1
TMEM179B	6	0.46346	3	3	7.466	1	0.11338	18.62619	4.7619	0	0	1
CXCR1	6	0.46346	3	3	9.18	1	0.11338	19.30952	4.85909	0	0	1
VNN2	3	0	1	3	5.533	2	0.11338	17.45952	4.61613	103.8333	164	0
PPP1CB	3	0	1	3	1.782	5	0.03968	3.5	0.29762	10	10	0
IL2RG	3	0.30779	2	3	4.838	3	0.15873	18.48333	4.87528	188	328	0.33333
CSF3R	2	0	1	2	8.093	1	0.15873	20.2	5.15063	10.63636	54	0
UGCG	2	0.30779	2	2	2.431	1	0.13228	13.93333	4.11403	0	0	1
CHGB	2	0.30779	2	2	3.926	1	0.13228	15.86667	4.47036	0	0	1
FBXO40	2	0	1	2	1.682	2	0.11338	11.82619	3.44995	96	166	0
DCUN1D2	2	0	1	2	2.144	3	0.13228	14.31667	4.19501	188	328	0
NUCB1	2	0.30779	2	2	3.932	1	0.13228	15.86667	4.47036	0	0	1
CSNK1D	2	0	1	2	1.651	2	0.03968	3	0.27778	6	6	0
SHC1	2	0.30779	2	2	2.384	1	0.13228	13.93333	4.11403	0	0	1
TNFRSF1A	2	0.30779	2	2	7.96	1	0.15873	19.06667	5.00486	0	0	1
HIF1A	2	0	1	2	4.667	4	0.15873	18.2	4.90768	276	486	0

ANGPT2	1	0	1	1	2.993	1	0.11338	14.44286	4.2436	0	0	0
DROSHA	1	0	1	1	1.235	1	0.03175	1	0.09524	0	0	0
AATF	1	0	1	1	1.235	1	0.03175	1	0.09524	0	0	0
S100A12	1	0	1	1	2.365	1	0.09921	12.80119	3.83868	0	0	0
AQP9	1	0	1	1	3.626	1	0.11338	14.59286	4.276	0	0	0
SELL	1	0	1	1	4.602	1	0.13228	16.41667	4.64853	0	0	0
RAC2	1	0	1	1	1.241	1	0.03175	1	0.09524	0	0	0
RALB	1	0	1	1	1.241	1	0.03175	1	0.09524	0	0	0
SERPINB1	1	0	1	1	5.298	1	0.11338	17.40952	4.74571	0	0	0
SLC4A1	1	0	1	1	1.211	1	0.03175	1	0.09524	0	0	0
AHSP	1	0	1	1	1.211	1	0.03175	1	0.09524	0	0	0
PPP1R3A	1	0	1	1	1.337	1	0.02646	2.33333	0.2381	0	0	0
RNF19B	1	0	1	1	1.368	1	0.09921	9.55595	2.6725	0	0	0
RPS8	1	0	1	1	1.37	1	0.02646	2.16667	0.21825	0	0	0
PPP3CB	1	0	1	1	1.342	1	0.02646	2.33333	0.2381	0	0	0
ADAMTS9	1	0	1	1	3.059	1	0.11338	14.44286	4.2436	0	0	0
PROK2	1	0	1	1	4.623	1	0.11338	16.72619	4.61613	0	0	0
IL1R2	1	0	1	1	4.48	1	0.15873	17.15	4.8105	0	0	0
NAMPT	1	0	1	1	1.226	1	0.03175	1	0.09524	0	0	0
PNP	1	0	1	1	1.226	1	0.03175	1	0.09524	0	0	0

Table A.5 The enriched pathways and diseases related with genes

Category	ID	Name	Source	p-value	q-value Bonfer-roni	q-value FDR B&H	q-value FDR B&Y	Hit Count in Query List	Hit Count in Genome	Hit in Query List
Disease	C0243026	Sepsis	DisGeNET Curated	1.73E-07	7.56E-05	7.56E-05	5.03E-04	6	510	FPR2,CLEC4D,CD177,ELANE,LCN2,PTX3
Disease	C0272175	Immune neutropenia	DisGeNET BeFree	2.04E-06	8.89E-04	4.45E-04	2.96E-03	2	4	CD177,ELANE
Disease	C0036690	Septicemia	DisGeNET Curated	3.99E-06	1.74E-03	5.81E-04	3.87E-03	5	461	FPR2,CD177,ELANE,LCN2,PTX3
Disease	C0085578	Thalassemia Minor	DisGeNET Curated	3.08E-05	1.35E-02	3.36E-03	2.24E-02	2	14	CD177,LCN2
Disease	C0005283	beta Thalassemia	DisGeNET Curated	4.51E-05	1.97E-02	3.74E-03	2.49E-02	3	120	CD177,ELANE,LCN2
Disease	C3841475	beta ⁺ Thalassemia	DisGeNET BeFree	5.47E-05	2.39E-02	3.74E-03	2.49E-02	3	128	CD177,ELANE,LCN2
Disease	C0026946	Mycoses	DisGeNET BeFree	6.27E-05	2.74E-02	3.74E-03	2.49E-02	3	134	CLEC4D,ELANE,PTX3
Disease	C0040028	Thrombocytopenia, Essential	DisGeNET Curated	6.84E-05	2.99E-02	3.74E-03	2.49E-02	3	138	CD177,LCN2,PTX3
Disease	C0023473	Myeloid Leukemia, Chronic	DisGeNET Curated	8.52E-05	3.72E-02	4.14E-03	2.75E-02	5	867	TCN1,CLEC4D,CD177,ELANE,LCN2
Disease	C0152031	Joint swelling	DisGeNET BeFree	1.88E-04	8.24E-02	7.93E-03	5.28E-02	2	34	ELANE,PTX3
Disease	C0032463	Polycythemia Vera	DisGeNET Curated	2.00E-04	8.72E-02	7.93E-03	5.28E-02	3	198	CD177,LCN2,PTX3
Disease	C0024117	Chronic Obstructive Airway Disease	DisGeNET Curated	2.57E-04	1.12E-01	9.34E-03	6.22E-02	4	566	CD177,ELANE,LCN2,PTX3
Disease	C0262655	Recurrent urinary tract infection	DisGeNET BeFree	4.09E-04	1.79E-01	1.38E-02	9.16E-02	2	50	LCN2,PTX3
Disease	C0004623	Bacterial Infections	DisGeNET Curated	4.44E-04	1.94E-01	1.39E-02	9.24E-02	3	260	ELANE,LCN2,PTX3
Disease	cv:C0221023	Cyclical neutropenia	Clinical Variations	6.14E-04	2.69E-01	1.45E-02	9.64E-02	1	1	ELANE
Disease	C3671688	Cyclic Hematopoiesis	DisGeNET Curated	6.14E-04	2.69E-01	1.45E-02	9.64E-02	1	1	ELANE
Disease	OMIN:162800	CYCLIC HEMATOPOIESIS	OMIM	6.14E-04	2.69E-01	1.45E-02	9.64E-02	1	1	ELANE
Disease	cv:C1859966	Severe congenital neutropenia autosomal dominant	Clinical Variations	6.14E-04	2.69E-01	1.45E-02	9.64E-02	1	1	ELANE
Disease	C3665444	Neutrophilia (disorder)	DisGeNET BeFree	6.29E-04	2.75E-01	1.45E-02	9.64E-02	2	62	CD177,ELANE
Disease	C0002875	Cooley's anemia	DisGeNET Curated	7.79E-04	3.40E-01	1.67E-02	1.11E-01	2	69	ELANE,LCN2
Disease	C0042029	Urinary tract infection	DisGeNET Curated	8.02E-04	3.50E-01	1.67E-02	1.11E-01	2	70	LCN2,PTX3
Disease	C0876973	Infectious disease of lung	DisGeNET BeFree	9.69E-04	4.24E-01	1.79E-02	1.19E-01	2	77	LCN2,PTX3
Disease	C0002726	Amyloidosis	DisGeNET Curated	1.08E-03	4.72E-01	1.79E-02	1.19E-01	4	826	FPR2,CD177,ELANE,PTX3
Disease	C0024115	Lung diseases	DisGeNET Curated	1.12E-03	4.89E-01	1.79E-02	1.19E-01	3	357	CLEC4D,ELANE,LCN2
Disease	C1274789	Ligneous conjunctivitis	DisGeNET Curated	1.23E-03	5.37E-01	1.79E-02	1.19E-01	1	2	ELANE
Disease	C0432562	Malignant lymphoma of spleen	DisGeNET BeFree	1.23E-03	5.37E-01	1.79E-02	1.19E-01	1	2	CLEC4D
Disease	C0221276	Relative erythrocytosis	DisGeNET BeFree	1.23E-03	5.37E-01	1.79E-02	1.19E-01	1	2	CD177
Disease	OMIN:202700	NEUTROPENIA, SEVERE CONGENITAL, AUTOSOMAL DOMINANT 1; SCN1	OMIM	1.23E-03	5.37E-01	1.79E-02	1.19E-01	1	2	ELANE
Disease	C0554309	Prerenal uremia syndrome	DisGeNET BeFree	1.23E-03	5.37E-01	1.79E-02	1.19E-01	1	2	LCN2
Disease	C0349208	Manic episode	DisGeNET BeFree	1.23E-03	5.37E-01	1.79E-02	1.19E-01	1	2	TCN1

Disease	C0003873	Rheumatoid Arthritis	DisGeNET Curated	1.65E-03	7.21E-01	2.18E-02	1.45E-01	5	1633	FPR2,ELANE, LRG1,LCN2,PTX3
Disease	C1968804	Plasminogen Deficiency, Type I	DisGeNET Curated	1.84E-03	8.05E-01	2.18E-02	1.45E-01	1	3	ELANE
Disease	C0004659	Bacteriuria	DisGeNET BeFree	1.84E-03	8.05E-01	2.18E-02	1.45E-01	1	3	LCN2
Disease	C0276088	Escherichia coli septicemia	DisGeNET BeFree	1.84E-03	8.05E-01	2.18E-02	1.45E-01	1	3	ELANE
Disease	C3714772	Recurrent fevers	DisGeNET BeFree	1.84E-03	8.05E-01	2.18E-02	1.45E-01	1	3	ELANE
Disease	C1858673	GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS, TYPE 2	DisGeNET Curated	1.84E-03	8.05E-01	2.18E-02	1.45E-01	1	3	ELANE
Disease	C1859966	Neutropenia, Severe Congenital, Autosomal Dominant 1	DisGeNET Curated	1.84E-03	8.05E-01	2.18E-02	1.45E-01	1	3	ELANE
Disease	C0042384	Vasculitis	DisGeNET Curated	2.00E-03	8.74E-01	2.30E-02	1.53E-01	2	111	ELANE,PTX3
Disease	C0031154	Peritonitis	DisGeNET Curated	2.41E-03	1.00E+00	2.52E-02	1.68E-01	2	122	FPR2,LCN2
Disease	C0022729	Klebsiella Infections	DisGeNET BeFree	2.45E-03	1.00E+00	2.52E-02	1.68E-01	1	4	LCN2
Disease	C0242528	Azotemia	DisGeNET Curated	2.45E-03	1.00E+00	2.52E-02	1.68E-01	1	4	LCN2
Disease	C0019188	Hepatitis, Animal	DisGeNET Curated	2.45E-03	1.00E+00	2.52E-02	1.68E-01	1	4	LCN2
Disease	C0023827	liposarcoma	DisGeNET Curated	2.53E-03	1.00E+00	2.52E-02	1.68E-01	2	125	TCN1,PTX3
Disease	C0023418	leukemia	DisGeNET Curated	2.84E-03	1.00E+00	2.52E-02	1.68E-01	5	1842	CLEC4D,CD177, ELANE,LCN2, PTX3
Disease	C0003850	Arteriosclerosis	DisGeNET Curated	2.85E-03	1.00E+00	2.52E-02	1.68E-01	4	1073	FPR2,CD177, LCN2,PTX3
Disease	C0004153	Atherosclerosis	DisGeNET Curated	2.92E-03	1.00E+00	2.52E-02	1.68E-01	4	1080	FPR2,CD177, LCN2,PTX3
Disease	C0577698	Exercise-induced angina	DisGeNET BeFree	3.07E-03	1.00E+00	2.52E-02	1.68E-01	1	5	PTX3
Disease	20090401:Tanaka	Folate pathway vitamins	GWAS	3.07E-03	1.00E+00	2.52E-02	1.68E-01	1	5	TCN1
Disease	C3839524	Anemia in malignant neoplastic disease	DisGeNET BeFree	3.07E-03	1.00E+00	2.52E-02	1.68E-01	1	5	LCN2
Disease	C2931027	Neutropenia, severe chronic	DisGeNET BeFree	3.07E-03	1.00E+00	2.52E-02	1.68E-01	1	5	ELANE
Disease	C3839957	Hereditary cystatin C amyloid angiopathy	DisGeNET BeFree	3.07E-03	1.00E+00	2.52E-02	1.68E-01	1	5	ELANE
Disease	C0457506	Reactive thrombocytosis	DisGeNET BeFree	3.07E-03	1.00E+00	2.52E-02	1.68E-01	1	5	CD177
Disease	C0030436	Parakeratosis	DisGeNET BeFree	3.07E-03	1.00E+00	2.52E-02	1.68E-01	1	5	LCN2
Disease	C1519670	Tumor Angiogenesis	DisGeNET BeFree	3.11E-03	1.00E+00	2.52E-02	1.68E-01	3	510	LRG1,LCN2,PTX3
Disease	C1136321	HIV-Associated Lipodystrophy Syndrome	DisGeNET Curated	3.68E-03	1.00E+00	2.87E-02	1.91E-01	1	6	TCN1
Disease	C0277524	Infectious colitis	DisGeNET BeFree	3.68E-03	1.00E+00	2.87E-02	1.91E-01	1	6	LCN2
Disease	C0003864	Arthritis	DisGeNET Curated	4.32E-03	1.00E+00	3.27E-02	2.18E-01	3	573	FPR2,ELANE,PTX3
Disease	C0009319	Colitis	DisGeNET Curated	4.34E-03	1.00E+00	3.27E-02	2.18E-01	3	574	ELANE,LRG1,LCN2
Disease	C0027947	Neutropenia	DisGeNET Curated	4.51E-03	1.00E+00	3.34E-02	2.22E-01	2	168	CD177,ELANE
Disease	C0398593	Specific granule deficiency	DisGeNET Curated	4.90E-03	1.00E+00	3.57E-02	2.38E-01	1	8	ELANE
Disease	C2004435	Vascular insufficiency of intestine	DisGeNET BeFree	5.52E-03	1.00E+00	3.83E-02	2.55E-01	1	9	PTX3
Disease	C0742132	cervical cancer metastasis	DisGeNET BeFree	5.52E-03	1.00E+00	3.83E-02	2.55E-01	1	9	LCN2
Disease	C0156149	Gastrointestinal tract vascular insufficiency	DisGeNET BeFree	5.52E-03	1.00E+00	3.83E-02	2.55E-01	1	9	PTX3
Disease	C0029877	Ear Inflammation	DisGeNET BeFree	6.13E-03	1.00E+00	4.12E-02	2.74E-01	1	10	PTX3

Disease	C0004030	Aspergillosis	DisGeNET Curated	6.13E-03	1.00E+00	4.12E-02	2.74E-01	1	10	PTX3
Disease	C0038454	Cerebrovascular accident	DisGeNET Curated	6.90E-03	1.00E+00	4.57E-02	3.04E-01	3	677	ELANE, MCEMP1, LCN2
Disease	C0014800	Erythroid hyperplasia	DisGeNET BeFree	7.35E-03	1.00E+00	4.59E-02	3.05E-01	1	12	CD177
Disease	C0035021	Relapsing Fever	DisGeNET BeFree	7.35E-03	1.00E+00	4.59E-02	3.05E-01	1	12	ELANE
Disease	C1456246	Bacteroides fragilis infection in conditions classified elsewhere and of unspecified site	DisGeNET BeFree	7.35E-03	1.00E+00	4.59E-02	3.05E-01	1	12	LCN2
Disease	C0948343	Transfusion-Related Acute Lung Injury	DisGeNET BeFree	7.35E-03	1.00E+00	4.59E-02	3.05E-01	1	12	CD177
Disease	C0006826	Malignant Neoplasms	DisGeNET Curated	7.58E-03	1.00E+00	4.67E-02	3.11E-01	4	1405	ELANE,LRG1, LCN2,PTX3
Disease	C0276096	Mastitis-metritis-agalactia syndrome	DisGeNET BeFree	7.96E-03	1.00E+00	4.76E-02	3.17E-01	1	13	LCN2
Disease	C0344315	Depressed mood	DisGeNET Curated	7.96E-03	1.00E+00	4.76E-02	3.17E-01	1	13	PTX3
Disease	C0010346	Crohn Disease	DisGeNET Curated	8.12E-03	1.00E+00	4.78E-02	3.19E-01	3	718	FPR2,LRG1, LCN2
Disease	C0042847	Vitamin B 12 Deficiency	DisGeNET Curated	8.57E-03	1.00E+00	4.78E-02	3.19E-01	1	14	TCN1
Disease	C0012813	Diverticulitis	DisGeNET BeFree	8.57E-03	1.00E+00	4.78E-02	3.19E-01	1	14	LCN2
Disease	C1318533	Secondary polycythemia	DisGeNET Curated	8.57E-03	1.00E+00	4.78E-02	3.19E-01	1	14	CD177
Disease	C0002888	Anemia, Megaloblastic	DisGeNET Curated	8.57E-03	1.00E+00	4.78E-02	3.19E-01	1	14	TCN1
Disease	C0497406	Overweight	DisGeNET Curated	8.65E-03	1.00E+00	4.78E-02	3.19E-01	2	235	LCN2,PTX3
Disease	C0027051	Myocardial Infarction	DisGeNET Curated	9.16E-03	1.00E+00	4.81E-02	3.20E-01	3	750	ELANE,LCN2, PTX3
Disease	C0010054	Coronary Arteriosclerosis	DisGeNET Curated	9.39E-03	1.00E+00	4.81E-02	3.20E-01	3	757	ELANE,LCN2, PTX3
Disease	C0009324	Ulcerative Colitis	DisGeNET Curated	9.43E-03	1.00E+00	4.81E-02	3.20E-01	3	758	FPR2,LRG1, LCN2
Disease	C0155626	Acute myocardial infarction	DisGeNET BeFree	9.44E-03	1.00E+00	4.81E-02	3.20E-01	2	246	LCN2,PTX3
Disease	C0018802	Congestive heart failure	DisGeNET Curated	9.46E-03	1.00E+00	4.81E-02	3.20E-01	3	759	ELANE,LCN2, PTX3
Disease	C0280099	Adult Solid Neoplasm	DisGeNET BeFree	9.79E-03	1.00E+00	4.81E-02	3.20E-01	1	16	ELANE
Disease	C2713442	Polyposis, Adenomatous Intestinal	DisGeNET Curated	9.79E-03	1.00E+00	4.81E-02	3.20E-01	1	16	LRG1
Disease	C0236053	Mucosal ulcer	DisGeNET BeFree	9.79E-03	1.00E+00	4.81E-02	3.20E-01	1	16	ELANE
Disease	C0742468	Central nervous system lesion	DisGeNET BeFree	9.79E-03	1.00E+00	4.81E-02	3.20E-01	1	16	LCN2
Disease	C2713443	Familial Intestinal Polyposis	DisGeNET Curated	9.79E-03	1.00E+00	4.81E-02	3.20E-01	1	16	LRG1
Disease	C0010068	Coronary heart disease	DisGeNET Curated	1.01E-02	1.00E+00	4.87E-02	3.24E-01	3	778	ELANE,LCN2, PTX3
Disease	C0948201	Alloimmunisation	DisGeNET BeFree	1.04E-02	1.00E+00	4.87E-02	3.24E-01	1	17	CD177
Disease	C0403814	Congenital bilateral aplasia of vas deferens	DisGeNET Curated	1.04E-02	1.00E+00	4.87E-02	3.24E-01	1	17	ELANE
Disease	C0029121	Oppositional Defiant Disorder	DisGeNET Curated	1.04E-02	1.00E+00	4.87E-02	3.24E-01	1	17	TCN1
Disease	C0022660	Kidney Failure, Acute	DisGeNET Curated	1.05E-02	1.00E+00	4.87E-02	3.24E-01	2	260	ELANE,LCN2
Disease	C0856169	Endothelial dysfunction	DisGeNET BeFree	1.06E-02	1.00E+00	4.87E-02	3.24E-01	2	261	LCN2,PTX3

Disease	C1956346	Coronary Artery Disease	DisGeNET Curated	1.09E-02	1.00E+00	4.96E-02	3.30E-01	3	800	ELANE,LCN2,PTX3
Disease	C0600041	Infective cystitis	DisGeNET BeFree	1.10E-02	1.00E+00	4.96E-02	3.30E-01	1	18	PTX3

Table A.6 DEGs between SC and control

symbol	logFC	AveExpr	t	PValue	adj.PVal	B
BMP5	-1.14917	3.491411	-12.7699	4.81E-14	9.06E-10	21.26324
MIR103A2	-1.19427	3.192519	-11.4251	8.90E-13	8.38E-09	18.65224
HBB	5.349245	9.589486	11.12618	1.75E-12	1.10E-08	18.03762
JUNB	1.654219	7.146345	9.93426	2.93E-11	1.38E-07	15.45761
MIR30E	-1.43626	2.776381	-9.78642	4.21E-11	1.58E-07	15.12291
CEBPD	1.265778	4.46663	9.337108	1.29E-10	4.04E-07	14.08562
PNRC1	0.852737	7.366001	8.867208	4.26E-10	1.15E-06	12.96854
FSD2	-2.24644	4.816767	-8.79813	5.09E-10	1.20E-06	12.80155
MIR99A	-1.08149	2.869388	-8.68224	6.88E-10	1.32E-06	12.51986
P2RY14	-1.77035	4.595705	-8.67567	7.00E-10	1.32E-06	12.50382
PDP1	-1.10323	7.279676	-8.59931	8.54E-10	1.46E-06	12.31706
SIK2	1.068499	6.517594	8.417009	1.38E-09	2.00E-06	11.86774
ISOC1	-0.8015	6.668696	-8.16306	2.70E-09	3.63E-06	11.2339
SNORA33	1.529854	4.561349	8.137631	2.89E-09	3.63E-06	11.16993
GAB2	0.902162	5.566889	7.948949	4.80E-09	5.65E-06	10.69246
RPPH1	1.703523	10.11987	7.879487	5.79E-09	6.41E-06	10.51544
GPAM	-1.19604	4.204961	-7.8117	6.96E-09	7.28E-06	10.34207
AGL	-0.84855	6.196222	-7.77392	7.71E-09	7.49E-06	10.24518
OSMR	1.283115	6.798044	7.762226	7.96E-09	7.49E-06	10.21515
CYB5D1	-0.84887	5.279301	-7.74447	8.35E-09	7.49E-06	10.16951
SMCO1	-2.7278	5.42071	-7.72509	8.80E-09	7.53E-06	10.11965
NDUFB3	-0.87743	7.299479	-7.63842	1.11E-08	9.13E-06	9.896122
ADAMTS9	2.290229	6.894961	7.563544	1.37E-08	1.07E-05	9.702189
HECW2	-1.06847	4.6748	-7.50778	1.59E-08	1.20E-05	9.55731
DHRS7C	-2.35742	4.256415	-7.48332	1.71E-08	1.24E-05	9.49361
HIVEP2	1.314952	6.707231	7.401625	2.14E-08	1.49E-05	9.280393
STAT3	1.143427	9.233847	7.346368	2.49E-08	1.67E-05	9.135703
RIPK2	1.24402	5.577041	7.302822	2.81E-08	1.82E-05	9.021413
TCEAL9	1.188806	7.041281	7.28389	2.96E-08	1.85E-05	8.971653
GJA1	-0.97317	8.625764	-7.27315	3.05E-08	1.85E-05	8.943416
TGIF1	1.081978	4.876739	7.189232	3.85E-08	2.20E-05	8.722221
ASB2	-1.45898	5.121704	-7.06711	5.41E-08	2.75E-05	8.398867
SMYD1	-1.7427	7.032966	-7.02367	6.11E-08	2.95E-05	8.283452
PDE7A	-0.94488	7.361244	-7.00834	6.38E-08	3.00E-05	8.242655
PPP2R3A	-1.08561	6.817181	-7.00014	6.52E-08	3.00E-05	8.220847
ETFDH	-0.77265	8.332458	-6.94193	7.68E-08	3.29E-05	8.065688
NDUFAB1	-0.76522	10.54959	-6.91603	8.26E-08	3.46E-05	7.996542
TIMMDC1	-0.78771	7.98943	-6.82937	1.05E-07	3.99E-05	7.764654
ETS2	1.336369	7.743867	6.827818	1.06E-07	3.99E-05	7.760494
NDUFB5	-0.88545	9.155845	-6.81956	1.08E-07	4.00E-05	7.738359

PDHB	-0.72452	7.98319	-6.79591	1.16E-07	4.19E-05	7.674923
USP2	-1.0653	6.302958	-6.77688	1.22E-07	4.29E-05	7.623812
GADD45B	2.105199	6.766639	6.774445	1.23E-07	4.29E-05	7.617282
TOMM34	0.712976	5.564372	6.759605	1.28E-07	4.39E-05	7.577414
DLK1	-0.70721	3.196265	-6.72073	1.43E-07	4.61E-05	7.472859
AAGAB	0.722924	4.034655	6.717892	1.44E-07	4.61E-05	7.465228
UTP4	0.883014	6.158175	6.705213	1.50E-07	4.70E-05	7.431095
SPRY1	0.900478	6.759073	6.656806	1.72E-07	5.07E-05	7.300635
CEMIP2	1.459228	5.039002	6.653554	1.73E-07	5.07E-05	7.291861
MAMDC2	-1.13529	4.346052	-6.6513	1.74E-07	5.07E-05	7.28579
GABARAPL1	0.868286	8.794723	6.637279	1.81E-07	5.18E-05	7.247945
GUCY1A1	-0.9755	6.214276	-6.60759	1.97E-07	5.47E-05	7.167757
LYRM7	-0.80148	6.391951	-6.53859	2.40E-07	6.46E-05	6.981118
MRPS33	-0.79648	7.115034	-6.50841	2.62E-07	6.75E-05	6.899342
PPIP5K2	-0.81537	5.938868	-6.50218	2.66E-07	6.78E-05	6.882441
ANGPT2	2.158216	5.467787	6.486004	2.79E-07	6.91E-05	6.838578
ATP5MC1	-0.70291	9.793046	-6.46212	2.99E-07	7.30E-05	6.773756
STC1	2.005771	6.354793	6.451982	3.07E-07	7.32E-05	6.746234
FASTKD1	-0.70105	6.147476	-6.44641	3.12E-07	7.35E-05	6.731106
TSPAN12	-1.14041	6.410284	-6.4052	3.51E-07	8.16E-05	6.619098
SOCS3	1.3687	4.017797	6.384725	3.72E-07	8.42E-05	6.563398
NT5C1A	-0.97662	3.511585	-6.38175	3.75E-07	8.42E-05	6.555307
CP	1.58654	3.677709	6.375905	3.82E-07	8.46E-05	6.539392
MRPL16	-0.73263	7.173026	-6.34209	4.21E-07	9.10E-05	6.447305
AIF1L	-1.00326	5.22805	-6.3284	4.37E-07	9.27E-05	6.409988
ACBD5	-0.89467	7.105248	-6.32783	4.38E-07	9.27E-05	6.408446
COQ3	-0.89741	4.537215	-6.29391	4.83E-07	9.88E-05	6.315956
RARRES1	2.185748	5.303619	6.261293	5.30E-07	0.000105	6.226926
HLF	-1.7985	5.130637	-6.26004	5.32E-07	0.000105	6.223513
DCUN1D2	-0.84373	5.875957	-6.21752	6.01E-07	0.000116	6.107336
SLC7A5	1.063364	3.665969	6.215514	6.04E-07	0.000116	6.101844
OR51E1	-0.92236	3.368802	-6.19169	6.47E-07	0.000122	6.036703
MTSS1	-0.8668	5.965209	-6.16344	7.02E-07	0.000128	5.9594
SSBP3	0.945046	5.999891	6.124879	7.84E-07	0.000141	5.853787
COLQ	0.882015	3.233576	6.11859	7.98E-07	0.000142	5.836554
NOD1	0.736866	3.911928	6.089196	8.69E-07	0.000153	5.755981
SCARNA10	2.638383	6.489574	6.082222	8.86E-07	0.000154	5.736855
PXMP2	-0.71313	5.02849	-6.07799	8.97E-07	0.000154	5.725241
IFITM1	0.709361	8.492146	6.070946	9.15E-07	0.000155	5.705928
BTG1	0.768238	7.170972	6.06365	9.35E-07	0.000156	5.685911
LRRC39	-1.42723	7.673683	-6.03583	1.01E-06	0.000164	5.609571
LMOD3	-0.95515	7.436293	-6.01519	1.07E-06	0.00017	5.552873
TMEM182	-1.6197	8.035881	-6.00055	1.12E-06	0.000176	5.51266
DEPP1	1.551201	5.852222	5.996172	1.14E-06	0.000177	5.500647
LONRF1	0.885313	4.079098	5.98685	1.17E-06	0.000179	5.475033
SNORD59B	-1.35478	3.788788	-5.98284	1.18E-06	0.000179	5.464006

SLC2A3	1.415427	5.952967	5.968894	1.23E-06	0.000181	5.425682
CD36	-0.83597	10.4218	-5.96092	1.26E-06	0.000183	5.403754
HIGD1B	-1.14869	6.691821	-5.94837	1.30E-06	0.000189	5.369265
TNFRSF11B	3.176602	5.614503	5.930443	1.37E-06	0.000193	5.319945
CMIP	0.716852	3.975537	5.92535	1.39E-06	0.000193	5.305936
VIT	-1.29231	4.328895	-5.92518	1.39E-06	0.000193	5.305474
PLA2G2A	1.692493	9.989563	5.924865	1.39E-06	0.000193	5.304601
IDI2-AS1	-0.95309	3.202327	-5.91928	1.42E-06	0.000193	5.289235
GPR34	-0.81012	4.21896	-5.91808	1.42E-06	0.000193	5.285925
NUPR1	0.869002	5.964429	5.909571	1.46E-06	0.000195	5.26252
BHLHE40	1.37629	7.165381	5.895471	1.52E-06	0.0002	5.223715
RASSF4	-0.79672	4.95836	-5.85942	1.68E-06	0.000216	5.124442
RARB	-0.81238	5.286362	-5.83594	1.80E-06	0.000221	5.059786
RRAD	2.386077	6.71599	5.834699	1.81E-06	0.000221	5.056357
RALB	0.750614	5.613253	5.834244	1.81E-06	0.000221	5.055102
NOLC1	0.735577	5.20969	5.824577	1.86E-06	0.000226	5.028465
NRBF2	0.854686	4.580671	5.815633	1.91E-06	0.000226	5.003819
TUBA3E	-1.30718	5.295476	-5.81323	1.92E-06	0.000226	4.997203
TIMM21	-1.01628	7.152648	-5.77784	2.13E-06	0.000246	4.899637
BCL6	0.836027	7.509433	5.775612	2.15E-06	0.000246	4.893491
FITM2	-1.27884	8.345239	-5.76994	2.18E-06	0.000249	4.877853
IFIT1	-1.12462	3.793645	-5.75915	2.25E-06	0.000254	4.848081
TTYH2	-0.77572	4.587751	-5.73916	2.38E-06	0.000262	4.792956
SNORD38B	1.438047	4.1431	5.726836	2.47E-06	0.000265	4.75895
RWDD2B	-0.94718	5.746315	-5.72631	2.47E-06	0.000265	4.757491
MVP	0.834368	3.654548	5.726079	2.48E-06	0.000265	4.756862
SNHG12	0.869504	4.650287	5.711929	2.58E-06	0.000269	4.717816
IL1R1	0.910547	6.740112	5.70981	2.60E-06	0.000269	4.711966
B4GALT5	0.84425	7.080565	5.708978	2.60E-06	0.000269	4.70967
DIAPH1	1.037853	6.075732	5.701734	2.66E-06	0.000273	4.68968
VDAC3	-0.72043	9.214565	-5.68693	2.77E-06	0.00028	4.648826
RNF122	1.544541	5.337246	5.684771	2.79E-06	0.00028	4.642857
ZNF682	-0.79531	3.431334	-5.68168	2.82E-06	0.00028	4.634316
CISH	1.431211	4.31189	5.677972	2.85E-06	0.000282	4.624088
PPP1R3A	-1.49952	7.628244	-5.66978	2.91E-06	0.000285	4.601464
POR	1.272563	5.382676	5.669033	2.92E-06	0.000285	4.599408
SNORA50A	1.003537	5.458167	5.654515	3.05E-06	0.000288	4.559322
SGPP2	-1.26634	4.469411	-5.65437	3.05E-06	0.000288	4.558929
CYP1B1	1.702799	6.221246	5.652543	3.06E-06	0.000288	4.553876
MID1	1.836183	5.156899	5.651234	3.07E-06	0.000288	4.550263
SNORD21	1.086413	4.280534	5.650117	3.08E-06	0.000288	4.547179
SSR3	-0.76255	7.80435	-5.6467	3.12E-06	0.000289	4.537737
KLHL7	-1.01373	6.518659	-5.6385	3.19E-06	0.000294	4.515098
MTHFD1L	0.701104	3.65001	5.632155	3.25E-06	0.000297	4.497574
TP53	0.761046	4.500472	5.608377	3.48E-06	0.000311	4.431895
TNFRSF1A	0.710832	7.266546	5.607392	3.49E-06	0.000311	4.429176

ACSL1	-0.84969	8.139482	-5.60623	3.50E-06	0.000311	4.425977
SYNE1	-0.77999	5.919212	-5.60553	3.51E-06	0.000311	4.424043
BLM	-0.79748	3.256616	-5.60432	3.52E-06	0.000311	4.420689
MIDN	0.881167	4.697495	5.579318	3.79E-06	0.000327	4.351614
IFI16	0.713327	6.852955	5.570985	3.88E-06	0.000331	4.328588
TENT5C	-1.06631	5.185511	-5.56094	3.99E-06	0.000334	4.300833
LRRN3	-0.93651	3.30373	-5.56013	4.00E-06	0.000334	4.298599
PLIN2	1.979663	8.247623	5.555003	4.06E-06	0.000335	4.284426
SNORA80E	1.519716	5.065061	5.534348	4.31E-06	0.000346	4.227343
MPPED2	-0.76354	3.762919	-5.52856	4.39E-06	0.000347	4.211338
PTDSS1	-0.74396	6.271625	-5.52856	4.39E-06	0.000347	4.211336
UGCG	0.824448	4.985024	5.525087	4.43E-06	0.000348	4.201745
SLCO2A1	1.267878	6.473234	5.515977	4.55E-06	0.000355	4.176568
SMAD3	1.138362	6.178727	5.486666	4.95E-06	0.000376	4.095543
SNORA23	1.711444	4.270546	5.448057	5.54E-06	0.000407	3.988807
RMRP	0.841634	10.09103	5.440525	5.66E-06	0.000411	3.967982
MLLT11	2.041588	7.632582	5.439486	5.68E-06	0.000411	3.965111
FAM155B	-0.72745	3.303642	-5.43059	5.83E-06	0.000419	3.940519
SCARNA17	0.884916	4.837402	5.426146	5.90E-06	0.000423	3.928228
NDUFA8	-0.7473	9.123428	-5.40651	6.25E-06	0.000436	3.87394
LRRC10	-0.83402	3.599382	-5.40509	6.27E-06	0.000436	3.869998
BCL3	0.945655	4.275754	5.393954	6.48E-06	0.000449	3.839219
SCARNA7	1.666043	5.436258	5.38692	6.61E-06	0.000456	3.819772
PYGM	-1.16216	5.423799	-5.3789	6.77E-06	0.00046	3.797596
TNFAIP1	1.014352	6.295265	5.37323	6.88E-06	0.000464	3.781921
EOGT	0.727257	6.297597	5.366577	7.02E-06	0.000471	3.763526
NPPA	3.262567	8.918426	5.3458	7.45E-06	0.000494	3.706079
THBS1	2.408601	9.044939	5.315101	8.15E-06	0.000534	3.621202
AQP9	0.721903	2.896899	5.313161	8.19E-06	0.000536	3.615839
PACS1	0.989403	6.867155	5.305787	8.37E-06	0.000541	3.595453
CRIM1	0.75708	7.183782	5.29749	8.57E-06	0.00055	3.572514
SLC25A40	-0.74343	6.101484	-5.29687	8.59E-06	0.00055	3.570797
PIK3R1	-1.06374	8.168767	-5.26393	9.45E-06	0.000589	3.479734
NAMPT	1.144649	9.388088	5.256541	9.65E-06	0.000594	3.45932
CASP4	0.780991	5.35765	5.25203	9.78E-06	0.0006	3.446852
NOX4	1.143428	4.117635	5.241161	1.01E-05	0.000613	3.416809
PLSCR1	0.730254	5.301097	5.240977	1.01E-05	0.000613	3.416301
APOO	-0.74421	6.934494	-5.23751	1.02E-05	0.000615	3.406706
COQ10A	-1.23406	7.963515	-5.23312	1.03E-05	0.000616	3.39458
SNORA68	1.122966	4.133705	5.230635	1.04E-05	0.000617	3.387717
CDK2	0.876582	4.802706	5.228963	1.05E-05	0.000617	3.383097
HBD	1.497604	3.415537	5.2122	1.10E-05	0.00064	3.336773
ZFP36	1.364279	7.913163	5.186004	1.18E-05	0.00068	3.264389
IL1RAP	1.228647	4.449051	5.179625	1.21E-05	0.000689	3.246766
CA14	-1.10065	3.366391	-5.16315	1.27E-05	0.000713	3.201249
SLC25A26	-0.71813	5.732546	-5.1482	1.32E-05	0.000739	3.159957

RTN4	0.961731	7.128083	5.147624	1.32E-05	0.000739	3.158369
LSMEM2	-1.00161	4.419846	-5.13308	1.38E-05	0.000758	3.118214
MRPS25	-0.78258	6.753227	-5.12168	1.43E-05	0.000781	3.086732
C1QTNF1	1.696597	6.235901	5.09979	1.52E-05	0.000825	3.026286
GRAMD1A	0.77651	4.633517	5.097096	1.53E-05	0.000829	3.01885
KLHL31	-1.27909	7.66346	-5.08156	1.60E-05	0.000859	2.975978
SHC1	0.739102	5.476122	5.079861	1.61E-05	0.000859	2.971277
PELI1	1.010483	5.231923	5.066068	1.68E-05	0.000887	2.933215
SLC25A30	-1.29037	7.413922	-5.05597	1.73E-05	0.000898	2.905346
INSYN1	-0.94877	5.103381	-5.05253	1.74E-05	0.000904	2.895872
TPM3P9	0.794253	5.061125	5.046004	1.78E-05	0.000912	2.877857
MID1P1	1.559564	4.695771	5.040832	1.80E-05	0.000916	2.86359
SH3RF1	0.706345	4.894847	5.038903	1.81E-05	0.000918	2.858269
RNU4-1	1.8258	4.516508	5.030039	1.86E-05	0.000932	2.833819
GOS2	-1.37441	5.482538	-5.00632	1.99E-05	0.000979	2.768422
ETV6	0.70739	4.979746	5.001907	2.02E-05	0.000979	2.756246
PTPN3	-1.03297	5.351632	-4.99952	2.03E-05	0.000979	2.749656
SLC25A20	-0.9529	5.200294	-4.99473	2.06E-05	0.000983	2.736449
SCN7A	-0.99702	6.475075	-4.98235	2.14E-05	0.001006	2.702332
ACTN1	0.989242	6.875694	4.976428	2.17E-05	0.001019	2.686018
RPGR	0.898688	4.508196	4.976049	2.18E-05	0.001019	2.684973
FNDC5	-0.85476	4.949046	-4.96832	2.23E-05	0.001035	2.663685
AKAP1	-0.9243	7.325492	-4.96746	2.23E-05	0.001035	2.661312
KLHL38	-2.05271	5.519249	-4.95316	2.32E-05	0.001063	2.621898
KLHL8	1.075233	5.690453	4.952336	2.33E-05	0.001063	2.619642
ACKR1	0.708316	4.05345	4.943158	2.39E-05	0.001081	2.594361
SELENOM	0.863981	6.481704	4.93965	2.42E-05	0.001089	2.5847
PM20D2	0.756013	5.241413	4.930842	2.48E-05	0.001112	2.560447
LDHA	0.721493	9.183429	4.928543	2.50E-05	0.001112	2.554118
HSD11B1	0.963385	3.583508	4.918899	2.57E-05	0.001135	2.527565
NREP	-1.30138	5.90526	-4.90557	2.67E-05	0.001174	2.49089
MYC	1.190319	6.605113	4.90277	2.69E-05	0.001181	2.483173
ALPL	0.909407	3.885364	4.899028	2.72E-05	0.001191	2.472875
IL4R	0.74054	3.297987	4.897856	2.73E-05	0.001192	2.469651
MYL7	-1.97009	9.968209	-4.88413	2.84E-05	0.001231	2.43188
S100A8	1.877033	8.631599	4.883414	2.84E-05	0.001231	2.429918
ADAM23	-0.81513	6.903819	-4.87815	2.89E-05	0.001243	2.415441
SCARNA5	1.225105	5.264626	4.875512	2.91E-05	0.001245	2.408182
RMDN2	1.071291	6.760834	4.863193	3.02E-05	0.001276	2.374305
GRAMD1B	2.046013	6.033227	4.851142	3.12E-05	0.001312	2.341174
SNORA5A	0.87834	7.734969	4.847534	3.16E-05	0.001312	2.331256
SFRP1	-0.94502	3.479078	-4.84743	3.16E-05	0.001312	2.330982
RNF19B	0.855795	5.004042	4.838184	3.24E-05	0.001342	2.305562
ARRDC3	0.969077	6.432587	4.834712	3.27E-05	0.001349	2.296021
PDZRN3	-0.70015	4.646227	-4.82908	3.33E-05	0.00136	2.280533
PNP	1.439417	5.81504	4.828447	3.33E-05	0.00136	2.278808

S100A9	1.583675	7.301953	4.807731	3.54E-05	0.001412	2.221906
YBX3	0.7487	10.26248	4.802799	3.59E-05	0.001423	2.208363
HES1	0.703491	3.526498	4.801549	3.60E-05	0.001423	2.204932
TOB1	-0.72358	6.99729	-4.78694	3.76E-05	0.001466	2.164837
ATP13A3	1.225047	7.65239	4.783181	3.80E-05	0.001475	2.154514
SEMA6D	-0.77021	3.738794	-4.77482	3.89E-05	0.001496	2.131567
GMPR	-0.94617	6.846303	-4.76415	4.01E-05	0.001527	2.102303
GCA	0.939212	4.870164	4.759365	4.07E-05	0.001539	2.089179
PGAM2	-0.7607	9.083216	-4.75331	4.14E-05	0.00156	2.072569
NAV1	-0.8345	6.776713	-4.7496	4.19E-05	0.00157	2.062389
AQP4	-1.56868	4.359712	-4.74622	4.23E-05	0.001582	2.053136
S100A12	2.159373	4.32642	4.742353	4.27E-05	0.001594	2.042535
CHRM2	-1.33259	5.670969	-4.74113	4.29E-05	0.001596	2.039173
S100A11	0.823432	9.024575	4.724657	4.50E-05	0.001658	1.994037
MAP1B	0.862839	8.702369	4.696794	4.87E-05	0.001765	1.917733
CHN2	-0.94601	5.020218	-4.6958	4.89E-05	0.001767	1.91502
NPC1	0.762168	4.729244	4.69058	4.96E-05	0.001776	1.900722
UQCRH	-0.93661	7.488696	-4.68803	5.00E-05	0.001784	1.893733
MS4A4A	-1.00034	4.408065	-4.6821	5.08E-05	0.001796	1.877529
TPCN1	-0.92	5.954535	-4.6775	5.15E-05	0.001814	1.864937
PTGIS	1.051109	5.521477	4.671091	5.25E-05	0.001814	1.847399
NNMT	0.84071	6.532896	4.670589	5.26E-05	0.001814	1.846026
HVCN1	1.053339	4.503526	4.670394	5.26E-05	0.001814	1.845494
NHLRC2	-0.71847	7.456698	-4.66722	5.31E-05	0.001827	1.836799
TGM2	1.007857	9.166943	4.665846	5.33E-05	0.001828	1.833056
LXN	0.705692	4.385704	4.647848	5.61E-05	0.001894	1.783848
CLIC6	-0.72551	3.6133	-4.64646	5.63E-05	0.001897	1.780065
SMC2	-0.73229	4.598507	-4.6453	5.65E-05	0.001897	1.776883
COQ5	-0.70995	5.902285	-4.63997	5.74E-05	0.001908	1.762317
EYA1	-0.83533	5.40442	-4.6302	5.90E-05	0.001941	1.735626
MLF1	-1.0435	6.866426	-4.62927	5.92E-05	0.001941	1.733093
MS4A6A	-1.0525	5.985359	-4.61737	6.13E-05	0.001968	1.700589
PRELID1	0.742737	6.871006	4.61282	6.21E-05	0.001984	1.68817
SEPTIN10	0.743693	6.21421	4.605741	6.33E-05	0.002011	1.668848
ASB8	-0.80143	6.665028	-4.59073	6.61E-05	0.002075	1.627892
SERPINE2	1.816236	6.234091	4.586487	6.69E-05	0.002089	1.616318
CYP4B1	-1.34509	5.34148	-4.57385	6.94E-05	0.00215	1.581875
GJC1	-0.72137	6.213884	-4.56467	7.13E-05	0.002186	1.556837
SNORA46	0.836537	3.638414	4.539241	7.67E-05	0.002314	1.487583
DGKD	1.24224	5.425509	4.532969	7.81E-05	0.002341	1.47051
DDX21	0.854006	6.298505	4.485334	8.95E-05	0.002584	1.340991
PHLDA1	0.9461	5.171761	4.472788	9.28E-05	0.002647	1.306923
PI15	1.644644	3.581763	4.46501	9.48E-05	0.002685	1.285811
FOSL2	0.819427	6.286993	4.453435	9.80E-05	0.002735	1.254406
SNORA75	1.845053	4.110226	4.447683	9.97E-05	0.002772	1.238807
PDK4	1.02805	11.35395	4.437638	0.000103	0.002832	1.211574

SNORD4B	1.02893	3.951173	4.434655	0.000103	0.002848	1.203489
SNORA3A	1.686753	4.039353	4.431461	0.000104	0.002861	1.194833
RNU4ATAC	1.205351	4.514364	4.425887	0.000106	0.00289	1.17973
PYGL	0.849083	4.876139	4.415426	0.000109	0.002953	1.151398
FNBP1L	0.709754	7.846135	4.414852	0.000109	0.002953	1.149845
CST7	0.828249	3.782551	4.409232	0.000111	0.002988	1.13463
PTPRE	0.710544	5.649085	4.403372	0.000113	0.003021	1.118769
PLCXD3	-0.8277	6.721054	-4.38128	0.00012	0.003168	1.059013
MFAP5	-1.12476	7.392306	-4.3789	0.000121	0.003185	1.052584
TMEM116	-0.733	6.527258	-4.37096	0.000124	0.003227	1.031134
ADIPOQ	-1.03598	3.06241	-4.35868	0.000128	0.003333	0.997955
SLC5A1	-1.44454	7.583028	-4.34948	0.000132	0.003407	0.973114
CSRP2	-0.79512	4.728012	-4.34479	0.000134	0.00344	0.960476
FBXO40	-1.71004	7.595432	-4.34451	0.000134	0.00344	0.959718
LSAMP	-0.79854	2.83474	-4.33758	0.000136	0.003491	0.941006
SLC26A2	0.934793	4.404478	4.32594	0.000141	0.003585	0.909626
SLC50A1	0.730571	4.981157	4.322859	0.000142	0.003598	0.90132
NPPB	3.578021	10.08898	4.32006	0.000143	0.003619	0.893777
ZPR1	0.712057	5.518717	4.318458	0.000144	0.003627	0.889461
CAVIN4	-1.39747	6.355311	-4.31497	0.000146	0.003654	0.880072
ELL2	1.094778	8.309079	4.309109	0.000148	0.0037	0.864275
PPDPF	0.813355	8.27451	4.305542	0.000149	0.003723	0.854671
TMEM88	-0.87198	7.358349	-4.30177	0.000151	0.00374	0.844511
CHI3L1	1.499155	3.86294	4.300912	0.000151	0.00374	0.842203
EFEMP1	1.010259	7.186777	4.267339	0.000167	0.003962	0.751907
RAB15	1.178083	4.050783	4.261516	0.000169	0.004017	0.736265
TIMP1	1.309261	9.783507	4.25531	0.000172	0.004074	0.719598
RDH10	0.834282	5.212868	4.253635	0.000173	0.004083	0.715099
SLCO5A1	0.710439	5.121915	4.252444	0.000174	0.00409	0.711902
HIST1H1E	-0.87914	7.655462	-4.25118	0.000174	0.004091	0.708504
PAIP2B	-0.839	7.28739	-4.24059	0.00018	0.004179	0.680089
PRICKLE1	-0.74116	4.503359	-4.2358	0.000182	0.0042	0.667236
ZDHHC2	0.774287	5.888437	4.198112	0.000203	0.004519	0.56627
CCL11	2.031386	6.794285	4.19017	0.000207	0.004591	0.545021
PROX1	-0.84352	6.027045	-4.19002	0.000207	0.004591	0.544615
RNU4-2	1.510202	3.779943	4.188988	0.000208	0.004599	0.54186
HILPDA	1.636402	4.104471	4.186842	0.000209	0.004619	0.536122
SEMA4B	0.809136	4.086099	4.186581	0.00021	0.004619	0.535424
MT1A	1.218541	7.898663	4.171816	0.000218	0.004769	0.495957
VCAN	1.189236	6.825931	4.165137	0.000223	0.004846	0.478117
ASB15	-1.5529	6.217123	-4.16287	0.000224	0.00487	0.472058
HRH2	1.061594	4.130943	4.153889	0.00023	0.00494	0.448092
NCEH1	-0.7106	6.893809	-4.15246	0.000231	0.004954	0.444264
SAT1	1.168401	9.254877	4.141324	0.000238	0.005071	0.414573
IL1RL1	1.861223	4.981396	4.127089	0.000248	0.005221	0.376634
LCN2	0.827089	3.151631	4.125795	0.000249	0.005234	0.373187

HAMP	1.466007	4.279773	4.125369	0.000249	0.005234	0.372053
PUM3	0.780855	4.968534	4.122687	0.000251	0.005268	0.364909
MT2A	0.805231	10.63312	4.121931	0.000251	0.005273	0.362898
CDCA7L	-0.86303	4.847928	-4.12116	0.000252	0.005273	0.360847
KCNK1	1.166302	5.124852	4.109361	0.000261	0.005415	0.329436
RPL22L1	0.759468	5.521375	4.099365	0.000268	0.005527	0.30285
SLC7A2	0.988351	6.066327	4.090646	0.000275	0.005628	0.279674
ENO1	0.721936	8.027079	4.085839	0.000278	0.005692	0.266901
PPRC1	0.795959	4.400769	4.083618	0.00028	0.005709	0.261001
THBS2	0.780516	5.57604	4.078717	0.000284	0.00576	0.247987
NRIP1	0.723507	6.651568	4.072495	0.000289	0.005834	0.231469
SYNPO2L	-1.05865	7.042482	-4.0619	0.000298	0.005922	0.203356
FNDC3A	0.809037	7.139526	4.055494	0.000303	0.00601	0.186377
FIGN	-0.77371	5.135552	-4.04985	0.000308	0.006074	0.171431
SERPINB1	1.181691	6.362022	4.048734	0.000309	0.006087	0.168462
C10orf71	-1.39624	6.037216	-4.04399	0.000313	0.006149	0.155891
GPR22	-1.12418	5.895309	-4.02837	0.000327	0.006372	0.114545
SP110	0.740195	4.842467	4.023328	0.000332	0.006429	0.101212
CCL2	1.801605	8.826422	4.018977	0.000336	0.006475	0.089707
MMP8	0.901526	2.998675	4.017925	0.000337	0.006475	0.086927
MPZL2	0.947957	3.920245	4.01638	0.000338	0.006477	0.082845
PPP1R1C	-0.96505	5.186745	-4.00143	0.000353	0.00667	0.043352
FLJ34503	-0.75269	3.019728	-3.99698	0.000357	0.006713	0.031592
ASB14	-0.81296	5.31951	-3.9891	0.000365	0.006817	0.010799
FLOT2	0.925397	6.141875	3.983686	0.000371	0.006894	-0.00346
PLOD2	0.809553	5.993012	3.959363	0.000397	0.007208	-0.06754
SNORD81	0.856224	7.227545	3.957413	0.000399	0.007241	-0.07266
TMEM165	0.736322	7.234975	3.940529	0.000418	0.007491	-0.11706
EBP	-0.78039	6.712009	-3.93153	0.000429	0.007607	-0.14068
MRC1	-1.17035	5.755459	-3.93113	0.00043	0.007609	-0.14174
SPATS2L	-0.78385	6.928806	-3.92622	0.000435	0.007692	-0.15464
VSNL1	-1.26079	5.241794	-3.92196	0.000441	0.007762	-0.16581
FAM118B	0.929676	6.216606	3.920534	0.000442	0.007784	-0.16956
SNORA60	1.173696	3.491347	3.916968	0.000447	0.007827	-0.17891
MPEG1	-0.89677	4.223133	-3.90953	0.000456	0.007954	-0.1984
ASCC2	0.775523	5.517814	3.906952	0.000459	0.008004	-0.20517
SNORA13	0.721661	3.138559	3.901339	0.000467	0.0081	-0.21987
SLC6A6	2.003068	6.391603	3.898942	0.00047	0.008147	-0.22615
RPP14	-0.72658	6.179331	-3.89733	0.000472	0.008176	-0.23038
SPHKAP	-0.91306	7.668306	-3.88653	0.000486	0.008367	-0.25863
TRIM8	0.709481	5.630904	3.885687	0.000488	0.008376	-0.26084
ASB11	-1.15594	5.867847	-3.88469	0.000489	0.008384	-0.26344
FGF12	-0.83729	7.963734	-3.87603	0.000501	0.008541	-0.28609
SLC11A1	0.770398	3.827324	3.874635	0.000503	0.008567	-0.28973
ERO1A	0.956082	5.924101	3.872054	0.000506	0.008606	-0.29648
LRRC8D	0.702039	4.604506	3.858351	0.000526	0.008851	-0.33226

SLC39A14	0.972426	7.36178	3.853565	0.000533	0.008926	-0.34474
SNORA52	0.953439	4.012742	3.837408	0.000557	0.009227	-0.38686
TC2N	-0.75791	4.206516	-3.82913	0.00057	0.009364	-0.40841
PFKM	-0.71514	8.040581	-3.81847	0.000587	0.009561	-0.43613
PN01	0.705492	4.241991	3.813889	0.000595	0.009642	-0.44805
ATP2B4	0.886201	8.305905	3.81133	0.000599	0.00966	-0.4547
SLC2A13	0.766973	4.464115	3.811033	0.0006	0.00966	-0.45547
CPM	-0.79928	5.198775	-3.79774	0.000622	0.009954	-0.49001
BTG2	1.003972	8.189828	3.752305	0.000705	0.010868	-0.60766
IER3	1.172181	5.732439	3.731924	0.000746	0.011301	-0.66028
ABCC5	0.98934	5.658722	3.716594	0.000778	0.011675	-0.69978
ANKRD2	-1.65253	6.745716	-3.70628	0.000801	0.011952	-0.72633
ABCD2	-0.87665	4.258881	-3.69969	0.000815	0.012124	-0.74328
COL4A1	0.766654	5.594325	3.683086	0.000853	0.012501	-0.78592
SERPINA1	1.024262	4.310401	3.678205	0.000865	0.01262	-0.79845
PLAUR	0.874283	4.195943	3.66846	0.000888	0.012862	-0.82343
ACACB	-0.87322	6.570272	-3.66753	0.00089	0.012885	-0.82581
DNAJC12	0.850542	3.815008	3.656781	0.000917	0.013178	-0.85334
SERPINE1	2.074159	6.110315	3.643895	0.00095	0.013557	-0.8863
SLC2A12	-0.74399	4.625163	-3.64278	0.000953	0.013589	-0.88916
FSTL3	0.930878	5.417185	3.637924	0.000965	0.0137	-0.90155
SNORA20	0.703516	3.486649	3.635793	0.000971	0.013746	-0.90699
UGDH	0.758077	5.572831	3.631415	0.000983	0.013891	-0.91817
RNU5E-1	1.348612	4.77299	3.621661	0.001009	0.014136	-0.94305
ZDHHC9	0.816038	6.75616	3.609678	0.001043	0.014499	-0.97359
ITGA3	0.771805	3.773796	3.59511	0.001085	0.014932	-1.01065
IP6K3	-0.75892	4.721835	-3.58942	0.001102	0.015033	-1.02512
ATP1A2	-0.97435	6.698072	-3.58824	0.001105	0.015059	-1.02812
SERPINA3	1.392925	7.234492	3.561564	0.001188	0.015791	-1.09577
ADAM19	1.284686	5.654686	3.553009	0.001216	0.016026	-1.11743
KCNJ2	-0.707	4.409597	-3.54617	0.001239	0.016259	-1.13473
IRF6	-0.78727	3.852887	-3.53962	0.001261	0.016434	-1.15129
NR4A3	1.204173	4.873335	3.527179	0.001304	0.01688	-1.18269
TIMP4	-0.70498	5.931541	-3.51004	0.001366	0.01737	-1.22587
HEY2	-1.13439	6.538458	-3.49193	0.001435	0.017916	-1.27142
RFTN2	-0.70952	4.287286	-3.49019	0.001441	0.017924	-1.27579
CD44	0.716964	6.083549	3.479205	0.001485	0.018283	-1.30335
USP54	0.784381	5.755154	3.477029	0.001493	0.018353	-1.30881
IGF1	0.975317	5.492557	3.473808	0.001506	0.018466	-1.31688
NUDT7	-0.78928	4.403721	-3.46571	0.001539	0.018785	-1.33717
PAPPA	0.802798	3.484865	3.454718	0.001586	0.019116	-1.36467
ZNF814	-0.73918	4.024055	-3.44083	0.001646	0.019665	-1.39937
BEX1	0.910294	3.387398	3.434694	0.001673	0.019893	-1.41467
MIR21	-0.98517	3.436867	-3.4232	0.001726	0.020244	-1.44332
ANGPTL4	0.799176	3.546059	3.408278	0.001796	0.020809	-1.48044
PTX3	1.637538	4.198992	3.403349	0.00182	0.021005	-1.49269

ADAMTS4	0.827024	4.000876	3.398902	0.001841	0.021145	-1.50373
LYVE1	-0.94119	7.581283	-3.39541	0.001859	0.021249	-1.51239
SRXN1	0.880806	6.219047	3.394717	0.001862	0.021253	-1.51412
LINC00260	0.947355	4.642371	3.380375	0.001935	0.02184	-1.54967
FLJ42393	1.015605	4.640474	3.356379	0.002062	0.022871	-1.60899
F13A1	-1.08665	6.439116	-3.34709	0.002114	0.023197	-1.63191
FAM180A	-1.04239	3.580591	-3.34161	0.002145	0.023414	-1.6454
FABP4	-1.10714	8.194291	-3.33658	0.002174	0.023592	-1.65779
ZNF385D	0.735183	4.732874	3.321073	0.002265	0.024332	-1.69593
SELL	0.741189	3.249977	3.315893	0.002296	0.024591	-1.70864
MT1M	0.969879	7.936429	3.303284	0.002374	0.025273	-1.73957
GRAMD4	1.066825	4.192418	3.299678	0.002397	0.025399	-1.7484
MEIS1	0.762171	6.694559	3.299479	0.002398	0.025399	-1.74889
CACNB2	-0.7928	7.183015	-3.29588	0.002421	0.025599	-1.7577
RIPOR2	0.718179	3.426576	3.294822	0.002428	0.025642	-1.76029
RAB3A	-0.78764	5.346587	-3.28429	0.002496	0.02616	-1.78605
CSF3R	0.712284	3.096932	3.277729	0.00254	0.026542	-1.80206
B3GALT2	-0.81812	6.913539	-3.27357	0.002568	0.026775	-1.81221
UCHL1	1.026291	4.416765	3.264886	0.002627	0.027183	-1.83338
TFPI2	1.203814	3.391057	3.256997	0.002683	0.027513	-1.85259
TUBA8	-0.71724	6.766852	-3.25575	0.002691	0.027558	-1.85562
SMIM5	-0.7697	3.529854	-3.25104	0.002725	0.027811	-1.86709
ANXA3	-0.76779	6.383845	-3.24977	0.002734	0.027859	-1.87018
JPH1	0.735727	5.421681	3.24741	0.002751	0.027972	-1.87591
TXLNB	-1.04795	8.273429	-3.24226	0.002789	0.028247	-1.88843
NEB	1.238856	3.663397	3.228248	0.002893	0.029002	-1.92241
HIF3A	-0.77932	5.654075	-3.22378	0.002927	0.029194	-1.93323
LOC101928841	-0.85062	5.089506	-3.21862	0.002967	0.02942	-1.94572
PPM1K	-1.10076	6.050895	-3.21703	0.002979	0.02951	-1.94957
C3orf52	1.163198	4.851907	3.198963	0.003124	0.030459	-1.99321
XIRP1	1.097724	9.391453	3.195003	0.003156	0.030617	-2.00276
ITGA5	0.965999	6.268625	3.188139	0.003213	0.031011	-2.0193
SLN	1.635635	4.317916	3.178597	0.003294	0.031679	-2.04227
PAPPA-AS1	0.751117	3.750575	3.17712	0.003307	0.031769	-2.04582
IL1R2	1.254728	4.95862	3.170732	0.003362	0.032072	-2.06117
FCN3	1.06674	5.639439	3.165163	0.003411	0.032387	-2.07454
SERPINH1	0.76292	4.991966	3.164114	0.003421	0.032401	-2.07705
RNASE6	-0.83163	5.395054	-3.15784	0.003477	0.032851	-2.09209
TBX5	-0.80515	6.818888	-3.15343	0.003517	0.033097	-2.10266
PPBP	1.088008	3.620816	3.129252	0.003745	0.034601	-2.16046
LDLR	0.961162	5.017498	3.116085	0.003875	0.035312	-2.19184
MT1F	0.750616	4.808381	3.108348	0.003953	0.035701	-2.21024
MCAM	0.731336	4.662976	3.089723	0.004148	0.036875	-2.25445
MBNL3	-0.83872	3.499475	-3.07892	0.004265	0.037614	-2.28002
CFB	0.724959	3.890383	3.05979	0.00448	0.038858	-2.32522
AQP1	-0.73912	6.474743	-3.04466	0.004657	0.039935	-2.36085

STRIP2	0.730856	4.811471	3.034629	0.004778	0.0405	-2.38442
EDIL3	-0.75022	3.669745	-3.03189	0.004812	0.040706	-2.39085
TMEM176A	0.804067	6.590605	3.017591	0.004991	0.041716	-2.42435
MT1X	0.795753	9.161469	3.006372	0.005136	0.042512	-2.45059
SACS	0.78289	5.399888	3.002876	0.005182	0.042742	-2.45875
RASSF5	0.852823	3.472903	2.979959	0.005493	0.0446	-2.51213
KCNIP2	-1.32593	6.273676	-2.97329	0.005587	0.044999	-2.52762
GUCA1C	-1.09387	3.605955	-2.96323	0.005732	0.04565	-2.55096
ICAM1	0.844998	4.149569	2.959992	0.005779	0.045914	-2.55846
SCD	-0.73782	3.701185	-2.95785	0.00581	0.046067	-2.56343
CORIN	-1.28536	6.050504	-2.95121	0.005909	0.046496	-2.57879
GCSAM	0.701905	3.474076	2.949404	0.005936	0.04663	-2.58296
CCDC141	-0.75294	6.785846	-2.92047	0.006386	0.049135	-2.64966