Original Article

Investigation of the Underlying Genes and Mechanism of Macrophage-Enriched Ruptured Atherosclerotic Plaques Using Bioinformatics Method

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Aim: The study aimed to identify the underlying differentially expressed genes (DEGs) and mechanism of macrophage-enriched rupture atherosclerotic plaque using bioinformatics methods.

Methods: GSE41571, which includes six stable samples and five ruptured atherosclerotic samples, was downloaded from the GEO database. After preprocessing, DEGs between ruptured and stable atherosclerotic samples were identified using LIMMA. Gene Ontology biological process (GO_BP) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses of DEGs were performed using the Database for Annotation, Visualization, and Integration Discovery (DAVID) online tool. Based on the STRING database, protein-protein interactions (PPIs) network among DEGs were constructed. Regulatory relationships between miRNAs/transcriptional factors (TFs) and target genes were predicted using Enrichr, and regulatory networks were visualized using Cytoscape.

Results: A total of 268 DEGs (64 up-regulated and 204 down-regulated DEGs) were identified between ruptured and stable samples. In the PPI network, collagen type Ⅲ alpha 1 chain (COL3A1), collagen type I alpha 2 chain (COL1A2), and asporin (ASPN) were more than 15 interaction degrees. In the miRNA-target network, miR21 was highlighted with highest degrees and *ASPN* could be targeted by miR21. Functional enrichment analysis showed that *COL3A1* and *COL1A2* were significantly enriched in extracellular matrix organization and cell adhesion GO_BP terms. Pre-platelet basic protein (*PPBP*) was the most significantly up-regulated gene in ruptured atherosclerotic samples and enriched in immune response and inflammatory response GO_BP terms.

Conclusions: Down-regulated *COL3A1*, *COL1A2* and *ASPN*, and up-regulated *PPBP* might perform critical promotional roles in atherosclerotic plaque rupture. Furthermore, miR21 might be potential target to prevent atherosclerotic rupture.

Key words: Atherosclerosis, Ruptured atherosclerotic plaque, Macrophages, Differentially Expressed Genes, Transcription factors, microRNA

Introduction

Atherosclerosis, the most common vascular disease, is the main cause of death of 17.5 million people annually[1]. Atherosclerosis (AS) is a chronic inflammatory disease characterized by medium- and large-sized atherosclerotic plaques on the vascular walls, which consists of two types: stable and ruptured plaques. Erosion and rupture of atherosclerotic plaques lead to atherosclerotic embolization, which contributes to the majority of acute coronary syndromes[2]. Until now, differences in cellular composition between ruptured and stable plaques have been well established[3], and the immune system has been identified to play a basic role in the initial and development of atherosclerosis, as well as the mechanism of unstable plaques, which are prone to rupture[4]. During plaque rupture, however, the specific molecular mechanisms of macrophage

involved in the rupture of atherosclerotic plaques are complex and not fully characterized.

Multiple gene expression studies have been performed between whole plaques and normal tissue. For example, visfatin is reported to function as an inflammatory mediator, which mediates destabilization of atherosclerotic plaques[5]. The formation of AS plaques can be inhibited by PRDM16 via enhancing the function of periaortic brown adipose tissue[6]. It has also been reported that the balance between inflammation and fibrosis plays a key role in the transition of atherosclerotic plaques from stable to rupture-prone[7]. A recent review study summarized that inflammation also promotes plaque calcification to regulate the progression and regression of atherosclerosis[8]. To further reveal the mechanism of macrophage-enriched plaque rupture, a transcriptome dataset numbered GSE41571 was deposited by Lee *et al.*, and it has revealed that FABP4 and leptin were significantly elevated in rupture atherosclerotic plaques, indicating that down-regulated adipocytokine/PPAR signaling might be a promising therapeutic potential for AS[3]. However, the potential regulatory mechanisms of transcription factors (TFs) and miRNAs involved in the progression of rupture have not been revealed.

In the current study, the dataset of GSE41571 was re-analyzed using bioinformatics methods, including differentially expressed genes (DEGs) screening, functional enrichment analysis, protein-protein interaction, and the regulatory relationship prediction between transcriptional factors (TF)/microRNAs (miRNAs) and DEGs. With these analyses, we hope to identify new insights for the understanding of macrophage-enriched ruptures in atherosclerotic plaques.

Materials and Methods

Data Resources

The mRNA expression profiles of GSE41571[3] (human), which was assayed on the platform of GPL570 [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array chip, were obtained from Gene Expression Omnibus (GEO) database (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE41571). A total of 11 macrophage-rich regions of carotid AS samples, including six stable samples and five ruptured samples, were isolated from patients undergoing surgery of the carotid artery stenosis at the Regional Neurosurgical Center, Newcastle-upon-Tyne. The Local Research Ethics Committee authorized construction of this dataset, and informed consents of all patients were obtained.

Data Preprocessing

The raw data of CEL profiles were downloaded and read using affy in R package[9] (Version: 1.50.0, http://www.bioconductor.org/packages/release/bioc/html/affy.html), and subsequently processed using the robust multi-array average method[10, 11], including background correction, normalization, and expression calculation. Furthermore, probes were annotated using the annotation profile provided by the platform, and unmatched probes were discarded. For multiple probes matched to one gene symbol, the mean values of probes were calculated as the final expression of the gene.

Identification of DEGs

After processed, DEGs between groups were screened out using the Linear Models for Microarray (LIMMA; Version: 3.30.3) affy in R package[12]. q-value between gene expressions was determined using the T test and adjusted using Benjamin Hochberg (BH) method. Those genes with the cut-off criteria of q-value <0.05 and |log$_2$ fold change (FC)| >1 were considered as DEGs.

Functional and Pathway Enrichment Analysis

The Gene Ontology (GO) term[13] and Kyoto Encyclopedia of Genes and Genomes (KEGG)[14] pathway enrichment analyses of DEGs were performed using the online tool of the DAVID, version: 6.8)[15] with the thresholds of count ≥ 2 and p-value <0.05.

To observe the function of DEGs visually, the ClueGO plugin (Version 2.2.6, http://apps.cytoscape.org/apps/ClueGO)[16] of Cytoscape software[17] was used to visualize GO biological processes (BPs) and KEGG pathways enriched for up- and down-regulated DEGs under the threshold of p-value <0.05.

PPI Network Analysis

Based on the Search tool for the retrieval of interacting genes/proteins (STRING)[18] online database (http://string-db.org/), PPIs among DEGs-encoded proteins were predicted with the threshold of PPI score (medium confidence) ≥ 0.4. Then, PPIs were visualized using Cytoscape software (version: 3.2.0, http://cytoscape.org/). The degree centrality, a network topology index, was used to analyze the scores of nodes in the network. The nodes with higher degree played an important role in PPI network, and might be key nodes. Nodes represent proteins encoded by DEGs, and degree is considered as the number of protein interaction pairs of a certain protein.

Subnet Module Analysis

Proteins produced by genes in the same module tend to have the same or similar function, and they act as a module to function in a same biological role. Using the plugin of MCODE (Multi-Contrast Delayed
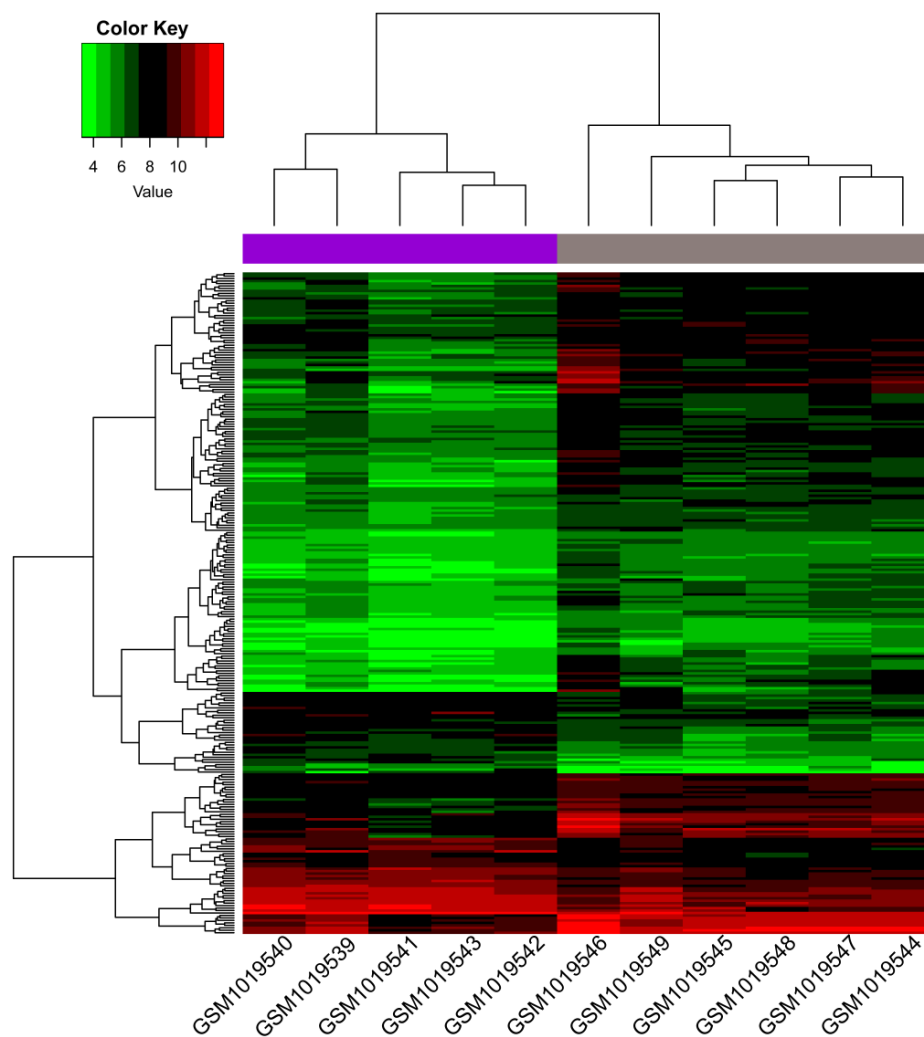
Fig. 1. Clustered heat map of DEGs. The abscissa represents different samples, and the ordinate represents different genes. The red boxes indicate up-regulated genes, and the green boxes indicate down-regulated genes.

DEGs: Differentially Expressed Genes.

Enhancement)[19)] in Cytoscape, the most significantly clustered modules in the network were analyzed. The score of each module was calculated using the MCODE algorithm. The higher the score of the module presented, the greater the number of close interactions and enrichments it possessed. Furthermore, GO and KEGG functional enrichments of modules with score ≥3 and node ≥5 were analyzed using DAVID.

Prediction of miRNA-Target Regulatory Networks

Regulatory relationships between miRNA and targeted-DEGs were predicted using Enrichr (http://amp. pharm.mssm.edu/Enrichr/)[20)] and adjusted by BH[21)] followed by the super geometric test. With the threshold of q-value <0.05, miRNA-target regulatory net-

work was visualized using the Cytoscape software.

Prediction of TF-Target Regulatory Networks

Based on TRANSFAC and JASPAR database, regulatory relationships between TFs and targeted-DEGs were predicted using Enrichr, and the TF-target regulatory networks were visualized by Cytoscape.

Results

Identification of DEGs

A total of 268 DEGs were identified in ruptured samples compared to stable samples, including 64 up-regulated genes and 204 down-regulated genes (**Supplementary Table 1**). COL1A2 and PPBP were the

Table 1. The top five results of functional enrichment analyses of up-regulated DEGs ranked by *P*-value

Term	Count	Gene	*P*-value
GO-BPs			
GO:0006955~immune response	9	*PPBP, IGKV1-17, CXCL3, NCF4, FCGR3A, IGKC, HLA-DMA, IGLC1, CD27*	4.82E-05
GO:0050853~B cell receptor signaling pathway	4	*CD38, IGKC, IGHM, IGLC1*	6.57E-04
GO:0038096~Fc-gamma receptor signaling pathway involved in phagocytosis	5	*IGKV1-17, HCK, FCGR3A, IGKC, IGLC1*	6.86E-04
GO:0006954~inflammatory response	7	*PPBP, CXCL3, HCK, S100A9, MGLL, CD27, CD180*	0.001192
GO:0050776~regulation of immune response	5	*LAIR1, IGKV1-17, FCGR3A, IGKC, IGLC1*	0.002385
KEGG pathways			
hsa04142:Lysosome	6	*AP1B1, GLA, GAA, NEU1, CTSA, ATP6V0B*	1.08E-04
hsa04060:Cytokine-cytokine receptor interaction	5	*LEP, PPBP, IL10RA, TNFRSF17, CD27*	0.013065
hsa04145:Phagosome	4	*NCF4, FCGR3A, HLA-DMA, ATP6V0B*	0.023255
hsa03320:PPAR signaling pathway	3	*CYP27A1, FABP4, PLTP*	0.02977
hsa05140:Leishmaniasis	3	*NCF4, FCGR3A, HLA-DMA*	0.033129

GO, Gene Ontology; BP, biological process; KEGG, Kyoto Encyclopedia of Genes and Genomes; DEGs, differentially expressed genes.

most significantly down-regulated and up-regulated genes in ruptured atherosclerotic samples, respectively. The Hierarchical clustering heat map of DEGs showed that these identified DEGs were well distinguished from the different kinds of samples (**Fig. 1**).

Functional Enrichment Analysis

GO functional and KEGG pathway analyses revealed that the up-regulated DEGs were significantly enriched in GO BP terms of the 'immune response' (*p*-value=4.82E-05), 'inflammatory response' (*p*-value= 0.001192) in GO BP, and 'Lysosome' pathway (*p*-value=1.08E-04) and 'Cytokine-cytokine receptor interaction pathways' (**Table 1**). The down-regulated DEGs identified in ruptured atherosclerotic plaque were enriched in GO_BP terms of 'extracellular matrix organization' (*p*-value=1.44E-08) and 'cell adhesion' (*p*-value=3.32E-15), and the KEGG pathways of 'focal adhesion' (*p*-value=7.82E-06) and 'ECM-receptor interaction' (**Table 2**).

PPI Network Analysis

A total of 154 nodes and 322 interactional pairs were included in the PPI network. Among them, only eight genes with degrees ≥15 in the PPI network were found, including type III alpha 1 chain (COL3A1), collagen type I alpha 2 chain (COL1A2), LUM, ACTA2, SPARC, ASPN, GNAI1 and COL5A2. Further, three functional subnet modules (mcode 1, mcode 2, and mcode 3) were selected from the PPI network. Specifically, mcode 1 consisted of 1 up-regulated node (LCP1) and 6 down-regulated nodes (**Fig. 2A**), mcode 2 was made up of five down-regulated nodes (e.g. COL3A1,

COL1A2 and COL5A2) (**Fig. 2B**), and mcode 3 consisted of twelve down-regulated nodes (e.g. ASPN) (**Fig. 2C**). In total, 5 nodes (e.g. COL3A1, COL1A2, COL5A2) of mcode 2 were mainly enriched in the "ECM-receptor interaction" (hsa04512) pathway, and nodes in mcode 3 was only enriched in the "Protein digestion and absorption" (hsa04974). Whereas, no pathway related to the nodes in mcode 1 was enriched.

Analysis of miRNA-Target and TF-Target Regulating Networks

In the miRNA-target regulating network, 114 nodes were detected, including 100 DEGs (e.g. COL3A1, ASPN) and 14 miRNAs (e.g. miR21), and miR21 was highlighted with highest degrees. Among these nodes involved in the PPI network, 310 regulatory relationships were identified between miRNAs and down-regulated DEGs (e.g. miR21-ASPN), but no regulatory relationship was observed between miRNA and the up-regulated DEGs (**Fig. 3**). One TF (TEA Domain Transcription Factor 2; TEAD2) was predicted to target 25 down-regulated DEGs (e.g. CCND1, BGN and COL8A1), and one TF (Spi-1 Proto-Oncogene; SFPI1) was predicted to regulate 10 up-regulated DEGs (e.g., PPBP) (**Fig. 4**).

Discussion

In the present study, 268 DEGs were identified in ruptured samples compared with stable samples. Specifically, *COL3A1* and *COL1A2* were important down-regulated genes, and *PPBP* was the most significant up-regulated gene in ruptured atherosclerotic samples.

Table 2. The top five results of functional enrichment analyses of down-regulated DEGs ranked by *P*-value

Term	Count	Gene	*P*-value
GO-BPs			
GO:0007155~cell adhesion	30	CTNNAL1, IGFBP7, ITGA10, SPOCK1, POSTN, CDH2, ITGBL1, ISLR, VCAM1, WISP1, ROBO1, FAT1, FAP, COL8A1, LAMB1, THBS2, DPT, PTPRK, MPDZ, PODXL, COL15A1, PPFIBP1, SSPN, TPBG, TNFAIP6, OMD, CX3CR1, MYH10, CDH11, AOC3	3.32E-15
GO:0030198~extracellular matrix organization	15	PDGFA, LUM, COL3A1, FBN1, ITGA10, POSTN, SPARC, ECM2, COL5A2, VCAM1, EGFLAM, BGN, COL1A2, LAMB1, COL8A1	1.44E-08
GO:0030199~collagen fibril organization	7	SFRP2, LUM, COL3A1, COL1A2, FOXC1, COL5A2, DPT	2.61E-06
GO:0001501~skeletal system development	10	AEBP1, COL3A1, FBN1, COL1A2, POSTN, FOXC1, EXT1, COL5A2, PRELP, CDH11	1.17E-05
GO:0001503~ossification	8	MGP, LRRC17, FOXC1, SPARC, EXT1, COL5A2, CDH11, TWIST1	1.77E-05
KEGG pathways			
hsa04510:Focal adhesion	11	VEGFC, CAV2, CCND1, PDGFA, COL3A1, COL1A2, ITGA10, LAMB1, THBS2, COL5A2, MYLK	7.82E-06
hsa04611:Platelet activation	7	GNAI1, COL3A1, COL1A2, GUCY1A3, COL5A2, MYLK, F2R	7.86E-04
hsa04512:ECM-receptor interaction	6	COL3A1, COL1A2, ITGA10, LAMB1, THBS2, COL5A2	8.27E-04
hsa04151:PI3K-Akt signaling pathway	10	VEGFC, CCND1, PDGFA, COL3A1, COL1A2, ITGA10, LAMB1, THBS2, COL5A2, F2R	0.002384
hsa04974:Protein digestion and absorption	5	COL21A1, COL3A1, COL1A2, COL15A1, COL5A2	0.00656

GO, Gene Ontology; BP, biological process; KEGG, Kyoto Encyclopedia of Genes and Genomes; DEGs, differentially expressed genes.

With a high degree in the PPI network, *ASPN* could be targeted by miR-21. Both *COL3A1* and *COL1A2* were enriched in the extracellular matrix organization and cell adhesion biological processes. *PPBP* was mostly enriched in immune and inflammatory response-related biological processes.

According to previous reports, balance between macrophage and fibrosis performs a critical role in the stability of atherosclerotic plaques[22, 23]. Ma *et al.* have demonstrated that deletion of matrix metalloproteinase (MMP)-28 in the infarct region induces a reduction in the expression of *COL1A1*, *COL3A1*, *COL5A1*, and *MMP-9*, which are closely associated with the progression of fibrosis[24]. Among these genes, *COL3A1* encodes the pre-α1 chain of type Ⅲ collagen, which has been identified to be related to the thickened intima of atherosclerotic lesions[25]. Mutation of the *COL3A1* gene is known to cause Ehlers-Danlos syndrome type Ⅳ (including rupture and stroke), which is related to early-onset occurrence of arterial ruptures[26]. Variants of *COL3A1* are risk factors for coronary and the recurrence of coronary events and artery disease in an Irish population[27]. The decrease in transcriptional activity of *COL3A1* results in reduced stability, rupture, and re-occlusion of small vessel plaques by reducing the production of type Ⅲ collagen[28]. *COL1A2* is the encod-

ing gene of the pro-alpha 2 chain of type Ⅰ collagen, which is a collagen to form fibril. Type Ⅰ collagen is the main component of the vessel wall and plays a key role in disease progression[29]. The content of collagen in atherosclerotic plaques and structural integrity of the fibrous cap are signs of plaque stability[30]. An unstable plaque that is prone to rupture is characterized by less collagen expression, a thinner fibrous cap, and a larger necrotic core[30]. In the current study, *COL3A1* and *COL1A2* were identified to be down-regulated in the macrophage-enriched rupture samples and interacted with each other. In coronary atherosclerosis, macrophages are reported to have cross talk between smooth muscle cells (SMCs), inhibiting the synthesis of MMPs and collagen proteins. This might be the potential explanation for the down-regulations of collagen related genes in rupture samples, but the in-depth mechanism for this crosstalk remains unclear. Improvement of plaque extracellular matrix (ECM) can enhance plaque morphology and stabilize lesions, indicating that change of ECM may be a potential new approach to improve atherosclerotic lesions[31-33]. In the current study, *COL3A1* and *COL1A2* were obviously enriched in the extracellular matrix organization and collagen fibril organization biological processes and focal adhesion and ECM-receptor interaction pathways. These find-
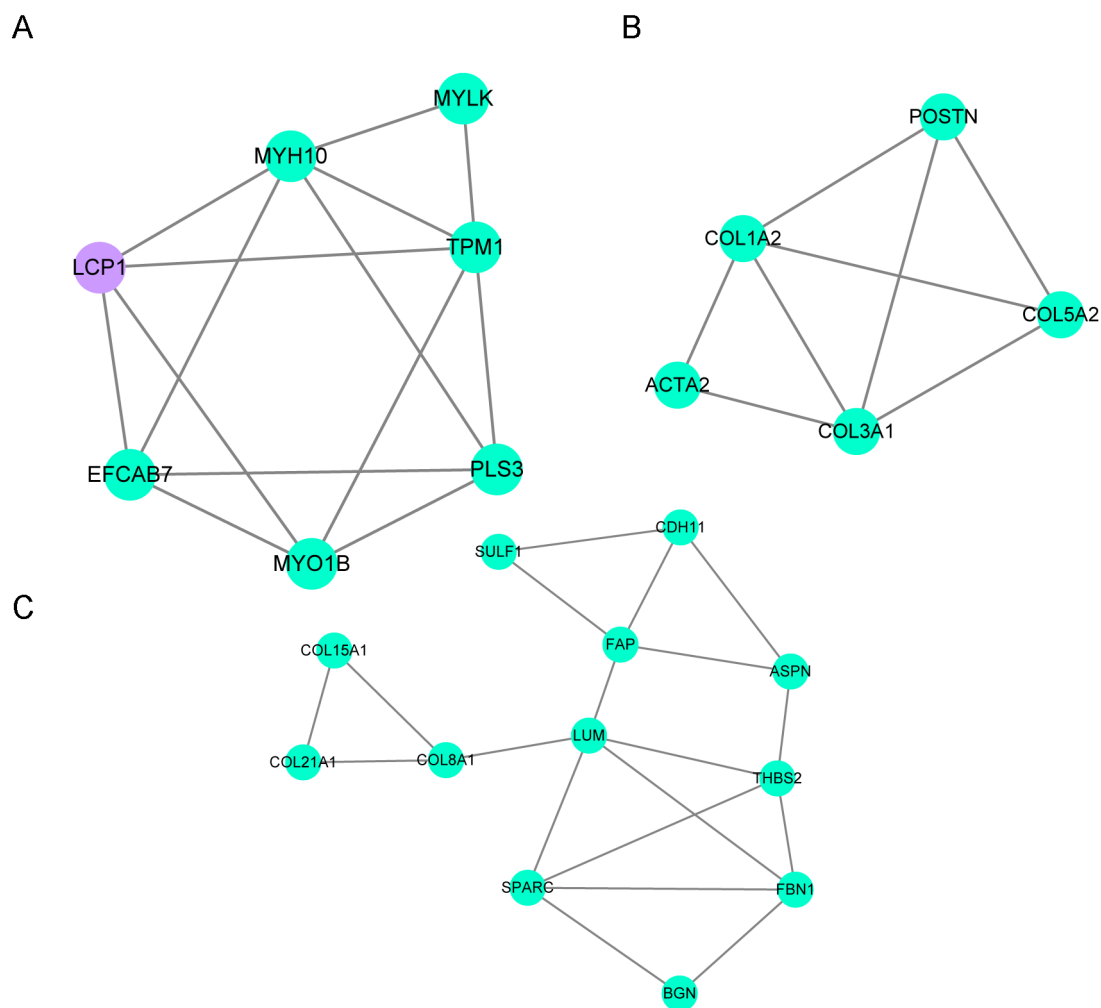
Fig. 2. Results of subnet module analysis of the PPI network. A: mcode 1; B: mcode 2; C: mcode 3. The green circles represent down-regulated DEG-encoded proteins and the purple circles represent up-regulated DEG-encoded proteins.

PPI: Protein-Protein Interaction; DEG, differentially expressed gene.

ings indicated that down-regulation of *COL3A1* and *COL1A2* might promote rupture via altering ECM components.

In the present study, among the 14 predicted miRNAs, miR21 had the most targeted-DEGs in the miRNA-target regulatory network. miR21 is implicated to play an important role in progression of various diseases including cancer, osteoarthritis, cardiovascular diseases and inflammation[34]. Liang *et al* have highlighted that the proatherosclerotic genes *COX2*, *VCAM1*, *ICAM1* and *MCP1* are regulated by miRNA-21 in macrophages of atherosclerotic plaques, indicating the importance of miRNA-21 in the development of atherosclerotic plaques[35]. It also reports that miR-21 may promote inflammation underlying atherogenesis in VSMCs and macrophages[36]. In our study,

ASPN was significantly down-regulated in macrophage-enriched rupture atherosclerotic plaques samples and predicted to be a target of miRNA-21. Asporin (*ASPN*) as a member of the small leucine-rich proteoglycan family, is a major non-collagen components of the ECM, and it has a possible role in calcification of collagen in atherosclerotic plaques[37], speculating that the low expression level of *ASPN* may reduce the calcification of collagen in atherosclerotic plaques. Interestingly, it has been demonstrated that unstable (known as non-calcified) plaques undergo thinning of the fibrous cap prior to rupture, possibly as a result of macrophages releasing proteolytic matrix-degrading enzymes which may degrade the fibrous cap[38]. What' more, another excellent study have supported that level of miR-21 in non-calcified coronary plaque patients' macrophages
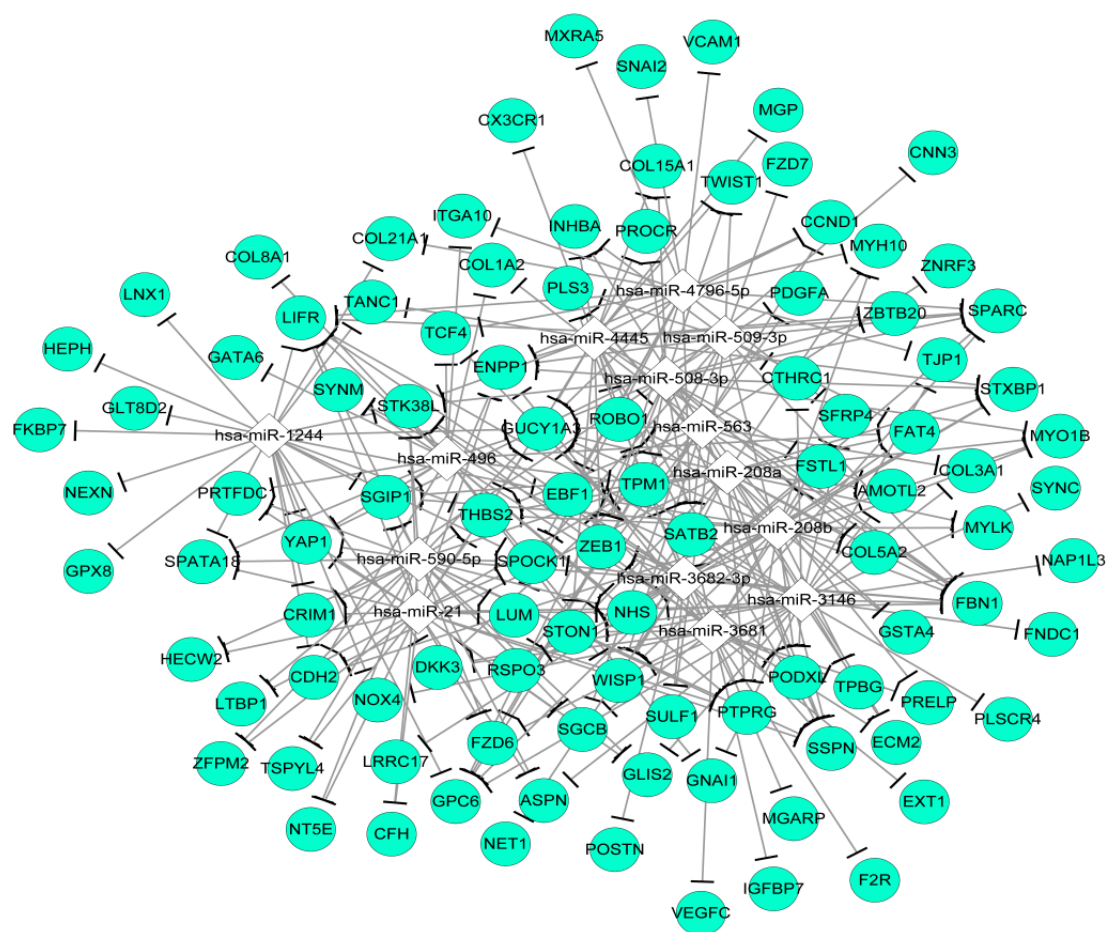
Fig. 3. MiR-target DEGs regulatory network. The diamond represents miRNA, and the green circle represents down-regulated DEGs.

DEGs: Differentially Expressed Genes

was higher than that in the coronary calcified groups, uncovering that miR-21 overexpression can enhance the instability of coronary atherosclerotic plaque in macrophages[39]. In consistent with our predicted regulatory pair, wang *et al* have suggested that *ASPN* may be regulated by miR-21 in the renal cortex of hypertensive patients[40]. Thus, it was speculated that miR-21 might play a role in calcification of collagen in macrophages of atherosclerotic plaques via regulating *ASPN*.

Pre-platelet basic protein (PPBP), also known as chemokine (Cxc Motif) Ligand 7 (CXCL7), is a platelet-derived growth factor that belongs to the CXC chemokine family. Chemokines play an important role on atherosclerosis development through attracting circulating inflammatory cells and stem/progenitor cells[41]. *PPBP* in connection with CTAP-IIII and CXCL4 regulate neutrophil adhesion and transendothelial migration[42]. As reported, monocyte-derived *CXCL7* can promote macrophages chemotaxis into the tumor micro-

environment[43]. *CXCL4*, *PPBP* structurally related gene, may affect the differentiation of monocytes and induces a specific M4 macrophage phenotype, which is associate with plaque instability[44]. In addition, *CXCL1*, an important paralog of *PPBP*, is up-regulated in carotid atherosclerotic plaques[45]. Similarly, our result revealed that *PPBP* was significantly up-regulated in ruptured atherosclerotic plaque samples, and among all up-regulated DEGs, its express change was greatest. Moreover, *PPBP* was significantly enriched in the immune and inflammatory response-related biological processes, which might be owing to the increased accumulation of macrophages. Therefore, it is deduced that accumulated macrophages might promote the expression of *PPBP*, increasing the destabilization of the atherosclerotic plaque.

However, some limitations should also be strengthened in this study. First, all the findings contained in this study were obtained using *in silico* methods, and
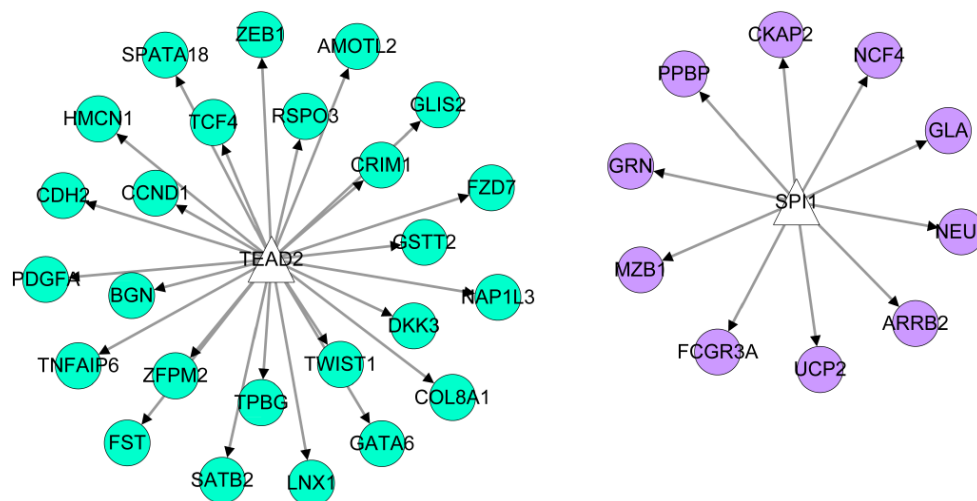
Fig. 4. TF-target DEGs regulatory network. The triangle represents TF, and the green circle and purple circle represent down-regulated and up-regulated DEGs, respectively.

TF: Transcription Factor; DEGs: Differentially Expressed Genes

the results experimental verifications were still deficient owing to insufficient tissue samples. Second, only small samples were included in this dataset, which might affect the values of these findings, or some other information might be ignored during these processes. Thus, a further analysis, combined experimental confirmation, and a larger sample size are required in future investigations.

Conclusions

In conclusion, findings in the current study demonstrated that the rupture of atherosclerotic plaques might be the result of imbalance between macrophages and fibrosis. Crosstalk between macrophages and SMCs may be involved in this process. Specifically, down-regulated *COL3A1*, *COL1A2* and *ASPN*, and up-regulated *PPBP* performed important promotional effects for the rupture of atherosclerotic plaques. Moreover, miR-21 was the potential up-stream regulators for *ASPN* and could serve as underlying targets for AS rupture prevention. These findings provide a theoretical basis for the future study of specific mechanisms of atherosclerotic rupture.

List of Abbreviations

atherosclerosis (AS); differentially expressed genes (DEGs); Gene Ontology biological process (GO_BP); Kyoto Encyclopedia of Genes and Genomes (KEGG); protein-protein interactions (PPIs); transcriptional factors (TFs); collagen type Ⅲ alpha 1 chain (COL3A1); collagen type I alpha 2 chain (COL1A2);

Asporin (ASPN); Pre-platelet basic protein (PPBP); TEA Domain Transcription Factor 2 (TEAD2); Spi-1 Proto-Oncogene (SFPI1); microRNAs (miRNAs); Gene Expression Omnibus (GEO); Benjamin Hochberg (BH); fold change (FC); Gene Ontology (GO); biological processes (BPs); Search tool for the retrieval of interacting genes/proteins (STRING); Multi-Contrast Delayed Enhancement (MCODE); matrix metalloproteinase (MMP); extracellular matrix (ECM); smooth muscle cells (SMCs); lipoprotein receptor-related protein 6 (LRP6)

Declarations

Ethics Approval and Consent to Participate

Construction of this dataset was authorized by the Local Research Ethics Committee.

Consent for Publication

Informed consents of all the patients were obtained.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Supplementary Table 1. The list of all differentially expressed genes

	logFC	AveExpr	t	P.Value	adj.P.Val	B
PIK3R6	1.2	6.319	8.201	3.85E-06	0.011196886	4.626
CEMIP	−1.25669178	7.687	−8.95594463	1.59E-06	0.011196886	5.387
CTNNAL1	−1.50635456	7.069	−8.76434724	1.98E-06	0.011196886	5.2
ROBO1	−2.70565648	8.496	−8.84771249	1.79E-06	0.011196886	5.282
ITGBL1	−3.36215802	7.681	−8.27010501	3.54E-06	0.011196886	4.699
METRNL	1.002	9.818	8.071	4.51E-06	0.011665271	4.487
CD38	1.565	6.27	7.222	1.33E-05	0.014239233	3.526
MPP1	1.133	10.398	7.139	1.49E-05	0.014239233	3.426
TMA16	−1.37306826	6.025	−7.14752281	1.47E-05	0.014239233	3.436
LNX1	−1.43840671	5.596	−7.69369652	7.22E-06	0.014239233	4.073
NT5E	−1.45802181	6.667	−7.10333002	1.56E-05	0.014239233	3.383
PMEPA1	−1.62651784	7.781	−6.9731982	1.86E-05	0.014239233	3.224
CRTAC1	−1.76339168	7.001	−7.42291778	1.02E-05	0.014239233	3.763
SULF1	−1.79939429	10.654	−7.25296984	1.28E-05	0.014239233	3.563
HECW2	−1.89456819	5.37	−7.158743	1.45E-05	0.014239233	3.45
GLIS2	−2.1429111	7.666	−7.34832308	1.13E-05	0.014239233	3.675
FAP	−2.28958226	8.494	−7.04661664	1.68E-05	0.014239233	3.314
LTBP2	−2.56032838	9.309	−7.53162444	8.88E-06	0.014239233	3.888
ASPN	−3.12774161	5.907	−6.95861939	1.90E-05	0.014239233	3.206
FNDC1	−3.6200187	7.689	−6.99541145	1.80E-05	0.014239233	3.251
COL21A1	−4.4469972	7.136	−7.14767824	1.47E-05	0.014239233	3.437
SLC7A8	1.015	6.912	6.849	2.20E-05	0.014542207	3.07
SKI	−1.01671528	5.422	−6.84693447	2.21E-05	0.014542207	3.067
SGCB	−1.18421525	6.196	−6.81390243	2.31E-05	0.014542207	3.026
LOC100132891	−1.82346745	6.17	−6.82874716	2.26E-05	0.014542207	3.045
FZD7	−2.02231618	6.228	−6.83837974	2.23E-05	0.014542207	3.057
MRAP2	−1.7051916	5.87	−6.78409852	2.41E-05	0.014749787	2.988
ZFPM2	−2.70450016	5.713	−6.72406374	2.62E-05	0.014749787	2.912
PLSCR4	−3.02986415	7.889	−6.71207272	2.66E-05	0.014749787	2.897
KDELC1	−1.07781756	5.894	−6.66357421	2.85E-05	0.014873881	2.835
EBF1	−1.93542721	5.188	−6.6531068	2.89E-05	0.014873881	2.822
EFCAB7	−1.26119539	5.316	−6.55903778	3.30E-05	0.015351409	2.701
LRRC17	−1.52743734	6.263	−6.5605111	3.29E-05	0.015351409	2.703
CTHRC1	−2.28289422	11.407	−6.52568507	3.46E-05	0.015776567	2.658
FKBP7	−1.08592784	5.062	−6.40842257	4.08E-05	0.016113508	2.504
LBH	−1.76630203	7.774	−6.47488815	3.71E-05	0.016113508	2.591
CRNDE	−1.81466313	6.371	−6.43567139	3.93E-05	0.016113508	2.54
RSPO3	−2.25938915	6.74	−6.41389175	4.05E-05	0.016113508	2.511
UCP2	1.046	10.197	6.356	4.40E-05	0.016270683	2.434
AFAP1	−1.21925021	5.084	−6.36304591	4.36E-05	0.016270683	2.444
FRMD6	−2.16411717	7.524	−6.37293311	4.30E-05	0.016270683	2.457
NTN4	−3.27525684	6.969	−6.29606061	4.80E-05	0.017460006	2.355
NCF4	1.354	8.239	6.285	4.88E-05	0.017468685	2.34
HEPH	−1.2555782	6.127	−6.26631153	5.01E-05	0.017676079	2.315
IGHM	1.254	6.413	6.147	5.97E-05	0.017810879	2.153

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
TPBG	− 1.14822882	6.065	− 6.15880954	5.86E-05	0.017810879	2.17
STK38L	− 1.26875147	9.209	− 6.15941448	5.86E-05	0.017810879	2.17
ART4	− 1.72536951	5.02	− 6.16575484	5.80E-05	0.017810879	2.179
KCNS3	− 1.91768639	6.684	− 6.19561586	5.55E-05	0.017810879	2.22
NAP1L3	− 2.51867182	5.597	− 6.19671351	5.54E-05	0.017810879	2.221
HMCN1	− 3.85610413	7.39	− 6.06690228	6.71E-05	0.018098086	2.044
PTPRK	− 1.50735965	5.155	− 6.03902761	6.99E-05	0.018288638	2.006
FBN1	− 2.24618566	8.156	− 6.03920907	6.99E-05	0.018288638	2.006
LOC100507165	− 1.26563477	6.349	− 5.99392548	7.48E-05	0.018713617	1.943
LUM	− 1.89877639	9.986	− 6.00525254	7.35E-05	0.018713617	1.959
PRSS23	− 1.40485461	7.92	− 5.96238674	7.83E-05	0.01915319	1.899
CTSLP8	1.546	6.208	5.91	8.48E-05	0.019311481	1.826
TRIM59	− 1.06753541	4.988	− 5.90024542	8.60E-05	0.019311481	1.813
THBS2	− 2.42982068	10.65	− 5.90527251	8.53E-05	0.019311481	1.82
FMO2	− 3.06556932	7.134	− 5.89211025	8.70E-05	0.019311481	1.801
EGFLAM	− 1.15809758	6.61	− 5.84266913	9.38E-05	0.020211564	1.732
SGIP1	− 2.38144236	5.731	− 5.81487254	9.78E-05	0.020508377	1.692
LAIR1	1.123	9.363	5.804	9.93E-05	0.020557983	1.678
ISLR	− 2.49728223	7.143	− 5.8014734	9.98E-05	0.020557983	1.674
FRY	− 1.05072072	5.327	− 5.74316552	0.000109014	0.02098725	1.591
ACTA2	− 2.91276358	5.63	− 5.74280218	0.000109074	0.02098725	1.59
STON1	− 1.1288534	5.259	− 5.70844297	0.00011494	0.021749286	1.541
RBMS3	− 1.20418414	4.754	− 5.70335452	0.000115837	0.021749286	1.534
SNX7	− 1.01351647	8.664	− 5.66744557	0.00012238	0.021750042	1.482
TRPC1	− 1.48467559	5.479	− 5.68361084	0.000119387	0.021750042	1.505
LOC102725271	− 2.08021698	6.195	− 5.6792456	0.000120188	0.021750042	1.499
FZD6	− 2.52508467	6.587	− 5.66876178	0.000122134	0.021750042	1.484
TMEM200A	− 2.65799647	7.649	− 5.68436322	0.00011925	0.021750042	1.506
LTBP1	− 2.66774268	9.446	− 5.63414494	0.000128799	0.021887182	1.434
HCK	1.027	10.062	5.586	0.00013864	0.022335508	1.365
WISP1	− 1.09763938	5.262	− 5.58419252	0.000139105	0.022335508	1.362
GPX8	− 2.09217016	7.453	− 5.58734641	0.000138429	0.022335508	1.366
ECM2	− 2.26273265	6.217	− 5.56641706	0.00014298	0.022645381	1.336
ZNF532	− 1.17796726	7.645	− 5.54560073	0.000147664	0.022803536	1.306
KCNT2	− 3.25602404	6.031	− 5.54458613	0.000147897	0.022803536	1.304
FSTL1	− 1.2961765	8.781	− 5.53364296	0.000150428	0.02299253	1.288
POSTN	− 2.00535336	7.828	− 5.5290006	0.000151516	0.02299253	1.281
LCP1	1.126	9.603	5.458	0.000169281	0.023576697	1.177
ASAP2	− 1.0195605	8.974	− 5.42846544	0.000177234	0.023576697	1.134
LOC100996668	− 1.03219502	5.509	− 5.43837456	0.000174505	0.023576697	1.148
LOXL1-AS1	− 1.29412144	4.801	− 5.46806046	0.000166593	0.023576697	1.192
PPIC	− 1.33677848	8.976	− 5.42561755	0.000178026	0.023576697	1.129
EXT1	− 1.34917431	6.22	− 5.49825972	0.000158932	0.023576697	1.236
GATA6	− 1.35281251	6.764	− 5.47930665	0.000163695	0.023576697	1.208
F2R	− 1.59271311	6.752	− 5.49532218	0.000159661	0.023576697	1.232

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
DKK3	− 1.86007416	6.333	− 5.45341254	0.000170448	0.023576697	1.17
MEIS2	− 1.94522503	6.595	− 5.48118849	0.000163216	0.023576697	1.211
LAMB1	− 2.36891793	7.601	− 5.41921172	0.000179823	0.023576697	1.12
MIR100HG	− 3.0403574	6.304	− 5.47572941	0.000164611	0.023576697	1.203
OXCT1	− 1.04892338	6.861	− 5.40242719	0.000184621	0.023747807	1.095
FAM114A1	− 1.19667178	8.182	− 5.37032694	0.00019418	0.023982939	1.047
ZNF415	− 1.64499095	5.195	− 5.36622657	0.000195438	0.023982939	1.041
LEP	2.268	6.42	5.34	0.00020371	0.024447275	1.002
LIFR	− 1.04740797	4.788	− 5.34280558	0.000202791	0.024447275	1.006
LIMCH1	− 1.44928729	5.869	− 5.34224492	0.000202971	0.024447275	1.006
GLA	1.142	11.256	5.328	0.000207585	0.024471802	0.984289808
SPOCK1	− 2.00207978	7.99	− 5.30897156	0.000213935	0.024471802	0.955807089
CAV2	− 1.71618358	6.47	− 5.2679935	0.000228303	0.025240194	0.894323182
CNN3	− 2.40155517	6.511	− 5.27633466	0.000225298	0.025240194	0.906860152
FABP4	2.335	5.645	5.246	0.000236293	0.025499036	0.861768833
FCGR3A	2.28	5.843	5.253	0.00023395	0.025499036	0.871203283
DHRS9	1.974	8.98	5.246	0.000236569	0.025499036	0.860667129
EVA1C	− 1.73126087	6.248	− 5.24772741	0.000235783	0.025499036	0.863816319
S100A9	1.814	9.17	5.231	0.000242257	0.02599181	0.83817444
TSPAN13	1.364	10.132	5.224	0.000245051	0.026121045	0.827316374
FIBIN	− 2.18712548	6.245	− 5.21228387	0.000249493	0.026283656	0.810304916
TMEM263	− 1.09452026	9.279	− 5.17428412	0.00026513	0.027145577	0.752711892
XG	− 1.14122656	5.25	− 5.1770576	0.000263954	0.027145577	0.756923192
ANO1	− 1.5220958	5.903	− 5.17976835	0.000262811	0.027145577	0.761038048
PLS3	− 2.61058898	10.003	− 5.16190948	0.000270443	0.027196827	0.733907168
IGLJ3	1.328	6.847	5.138	0.000280903	0.027589235	0.697929449
COL8A1	− 1.59954307	5.177	− 5.10344528	0.000297106	0.028177964	0.644736003
PODXL	− 2.5532906	8.65	− 5.10308659	0.000297278	0.028177964	0.644187253
CPE	− 2.41341692	6.49	− 5.08342649	0.000306862	0.028692184	0.614078827
MGP	− 2.7960331	7.892	− 5.06861727	0.000314295	0.029120038	0.591359135
PPBP	2.977	4.934	5.047	0.000325516	0.029568025	0.558054325
LINC00847	1.701	6.722	5	0.000351428	0.029568025	0.485294566
CKAP2	1.444	6.347	5.046	0.000326105	0.029568025	0.556335592
NINJ1	1.227	9.489	5.017	0.00034164	0.029568025	0.512134064
ZNF385A	1.002	7.307	5.015	0.000342894	0.029568025	0.50865254
TCF4	− 1.11012014	8.861	− 5.03410741	0.000332364	0.029568025	0.538282068
PRELP	− 1.83415382	8.551	− 5.00604766	0.000347861	0.029568025	0.494988219
C1R	− 1.86165559	9.136	− 5.04079479	0.000328779	0.029568025	0.548582002
GLT8D2	− 1.93529812	6.747	− 4.99897494	0.000351886	0.029568025	0.484056257
TMEM47	− 2.65208148	7.739	− 5.01707979	0.000341679	0.029568025	0.512024529
NEXN	− 2.73532684	6.243	− 5.03303355	0.000332943	0.029568025	0.53662745
AK021804	− 3.30885199	7.223	− 5.03233933	0.000333318	0.029568025	0.535557691
CRIM1	− 1.84112926	8.548	− 4.97768255	0.000364302	0.030183899	0.451098671
VCAM1	− 1.74604498	11.444	− 4.97321252	0.000366966	0.030189802	0.444170766
TSPYL4	− 1.16572958	8.755	− 4.95426541	0.000378491	0.030398027	0.41477112

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
FAT1	− 2.46760386	8.673	− 4.95239161	0.000379651	0.030398027	0.411860598
DNM3OS	− 2.26298358	5.665	− 4.94189258	0.000386222	0.030514411	0.395542649
SLC37A3	− 1.00679181	7.362	− 4.90755169	0.000408561	0.031189135	0.342050316
GNAI1	− 1.02458618	4.511	− 4.90353054	0.000411265	0.031189135	0.335774788
STXBP1	− 1.06233296	7.563	− 4.90389178	0.000411021	0.031189135	0.336338656
NHS	− 1.18994264	5.633	− 4.90527988	0.000410086	0.031189135	0.338505158
GRN	1.017	12.203	4.901	0.000412639	0.031191784	0.332599348
TNFAIP6	− 2.22807951	7.13	− 4.86846811	0.000435649	0.031943596	0.280950449
ZBTB20	− 1.00515779	6.98	− 4.84421694	0.000453401	0.03248024	0.242921225
SUGCT	− 1.88509353	7.086	− 4.84428645	0.000453349	0.03248024	0.243030364
CDH11	− 1.95194678	7.012	− 4.84519063	0.000452674	0.03248024	0.244449829
KIAA1377	− 1.11080072	4.659	− 4.82196057	0.000470362	0.032662868	0.20794168
CCND1	− 1.15263195	8.102	− 4.8216234	0.000470624	0.032662868	0.207411186
CDH2	− 1.2169333	7.663	− 4.8223331	0.000470072	0.032662868	0.208527793
NOX4	− 1.82320944	4.658	− 4.82715307	0.000466346	0.032662868	0.216109247
HMOX1	2.226	11.122	4.813	0.000477479	0.032773348	0.193633653
IL10RA	1.003	10.987	4.812	0.000478063	0.032773348	0.192469301
BICC1	− 1.10999716	4.796	− 4.79730384	0.000489933	0.032967077	0.169102285
AX747132	− 1.48765545	5.276	− 4.78862768	0.000497021	0.03306183	0.15541382
SFRP2	− 3.62509444	8.232	− 4.78137924	0.000503025	0.033365917	0.143969241
ARRB2	1.21	8.361	4.759	0.000521784	0.033462477	0.109069249
SPATA18	− 1.01167048	6.085	− 4.7517964	0.000528332	0.033462477	0.097179376
PRTFDC1	− 1.20002167	5.839	− 4.75113323	0.000528915	0.033462477	0.096128966
HEG1	− 1.29863636	9.213	− 4.75486385	0.000525647	0.033462477	0.10203709
PCDHGA4	− 1.61801494	4.893	− 4.76503003	0.00051685	0.033462477	0.11812655
COL1A2	− 2.23065822	10.887	− 4.75182652	0.000528306	0.033462477	0.097227086
MYH10	− 2.4727541	7.291	− 4.75829436	0.000522661	0.033462477	0.107468095
SLC48A1	1.098	7.003	4.744	0.000535212	0.033625891	0.084843842
PTPRG	− 1.06299347	4.626	− 4.72336071	0.00055392	0.034040944	0.052081228
PDGFA	− 1.20814415	7.245	− 4.7231203	0.000554141	0.034040944	0.051699445
STEAP1	− 1.59703261	7.015	− 4.71504336	0.000561647	0.034411224	0.03886755
TPM1	− 1.28919304	7.279	− 4.71171411	0.000564772	0.03441254	0.033575558
NEU1	1.14	8.864	4.701	0.000575252	0.034515567	0.016035637
CX3CR1	− 1.15611971	6.078	− 4.69985497	0.000576051	0.034515567	0.014711631
RP4-614O4	− 1.30864069	5.283	− 4.69918825	0.000576693	0.034515567	0.01365048
GUCY1A3	− 2.45288651	6.228	− 4.69733727	0.000578476	0.034533555	0.010704154
DPT	− 2.10253648	6.383	− 4.68924907	0.000586339	0.034865462	− 0.002176312
COL5A2	− 2.51114645	9.242	− 4.68842114	0.00058715	0.034865462	− 0.003495332
MZB1	2.34	6.786	4.665	0.00061014	0.035032694	− 0.040144013
ATP6V0B	1.249	10.161	4.67	0.000605709	0.035032694	− 0.033189336
FERMT2	− 1.32252556	6.945	− 4.66808806	0.000607445	0.035032694	− 0.035920518
YAP1	− 1.72909066	6.431	− 4.66877616	0.000606747	0.035032694	− 0.034822218
EML1	− 1.99655211	5.432	− 4.66075832	0.000614941	0.035032694	− 0.047624057
CFH	− 2.1218776	10.83	− 4.67777279	0.000597689	0.035032694	− 0.020468742
2018/3/2	− 1.049441	6.229	− 4.64018199	0.000636504	0.035582405	− 0.080520385

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
IGFBP7	− 1.17251974	8.893	− 4.61773173	0.000660938	0.036207263	− 0.116482484
DZIP1	− 1.21446462	5.069	− 4.61329159	0.000665885	0.036207263	− 0.123603551
IQCJ-SCHIP1	− 1.89678603	7.193	− 4.59387208	0.000687985	0.036631536	− 0.154781644
TAF1A	− 1.29817562	5.537	− 4.57505232	0.000710136	0.037323023	− 0.185048194
MXRA5	− 2.08246518	9.942	− 4.5760163	0.000708983	0.037323023	− 0.183496667
MYO1B	− 1.06000364	5.771	− 4.56172834	0.000726268	0.037659193	− 0.206506663
SLCO2B1	1.319	8.457	4.533	0.000762207	0.038274727	− 0.252652647
GSTT2	− 1.10875678	6.235	− 4.53840847	0.000755434	0.038274727	− 0.244123997
AEBP1	− 2.35590453	10.096	− 4.52961448	0.000766748	0.038274727	− 0.25832946
FCGRT	1.177	10.833	4.52	0.000778957	0.038504641	− 0.273426586
FAT4	− 2.56303105	6.048	− 4.51762232	0.000782464	0.038596008	− 0.27771853
INHBA	− 1.86991676	6.789	− 4.51503663	0.000785896	0.038683361	− 0.281901738
IGKV1-17	2.579	7.067	4.507	0.00079641	0.038894789	− 0.294602761
CYP27A1	1.326	11.108	4.498	0.000808921	0.039131153	− 0.30950161
LOC100506119	1.01	7.294	4.488	0.000822133	0.039303695	− 0.324987906
VEGFC	− 1.83703081	7.396	− 4.48856265	0.000821959	0.039303695	− 0.324785545
GAA	1.167	9.206	4.473	0.000843911	0.039994585	− 0.349981918
NFIB	− 1.32832364	5.712	− 4.45439285	0.00087108	0.040260819	− 0.38027823
SERTAD4	− 1.21609373	4.817	− 4.44402046	0.00088659	0.040401598	− 0.397154852
PLTP	1.311	10.929	4.432	0.000904488	0.040436634	− 0.416267419
CTSA	1.163	10.809	4.441	0.000890772	0.040436634	− 0.401654419
SLC16A4	− 1.39699797	4.694	− 4.42089439	0.00092222	0.040517383	− 0.434835104
FOXC1	− 2.12951548	8.291	− 4.42836534	0.000910549	0.040517383	− 0.422654485
IGKV1OR2-108	1.868	7.811	4.397	0.000960932	0.040756283	− 0.47416657
TJP1	− 1.08938082	6.622	− 4.40604957	0.000945876	0.040756283	− 0.459060347
ZNRF3	− 1.12957808	5.084	− 4.39928713	0.000956861	0.040756283	− 0.470105748
MPDZ	− 1.54103226	6.522	− 4.40894973	0.000941205	0.040756283	− 0.45432526
NET1	− 1.60153131	7.662	− 4.39586793	0.000962467	0.040756283	− 0.475692803
SNAI2	− 2.33153198	6.709	− 4.39421282	0.000965192	0.040756283	− 0.478397851
TANC1	− 1.04522496	5.558	− 4.38674571	0.000977589	0.040935653	− 0.490606346
IGKC	1.285	6.009	4.382	0.000985827	0.040965943	− 0.498633937
ACOT13	1.03	7.829	4.375	0.000997539	0.040965943	− 0.509933389
SPARC	− 1.20354323	11.219	− 4.3753052	0.000996905	0.040965943	− 0.509325556
GSTA4	− 1.29851562	6.86	− 4.36613168	0.001012682	0.040965943	− 0.524347965
ZBTB8A	− 1.37631649	7.052	− 4.37997542	0.000988972	0.040965943	− 0.50168195
FST	− 1.76779273	6.563	− 4.36991914	0.001006137	0.040965943	− 0.51814434
TWIST1	− 2.11250906	7.358	− 4.36900418	0.001007714	0.040965943	− 0.519642824
AOC3	− 2.28787858	7.915	− 4.3647634	0.001015057	0.040965943	− 0.52658959
ATL1	− 1.00687259	6.814	− 4.3604407	0.0010226	0.041059108	− 0.533672997
CRISPLD1	− 3.53397277	5.399	− 4.35427774	0.001033455	0.041200168	− 0.543776176
SSPN	− 1.17667481	5.806	− 4.35112305	0.001039058	0.041292889	− 0.548949711
PPP1R15A	1.035	7.244	4.335	0.001068043	0.041862246	− 0.575277661
MGLL	1.074	10.068	4.323	0.001090989	0.042231298	− 0.595619862
CFHR2	− 1.05882399	6.425	− 4.3235495	0.001089399	0.042231298	− 0.594224097
AMOTL2	− 2.27119759	7.063	− 4.3168058	0.001102093	0.04241147	− 0.605311898

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
TNFRSF17	2.009	4.822	4.298	0.001138401	0.043046977	−0.636334631
SLC24A3	−1.37012793	6.638	−4.29952451	0.001135333	0.043046977	−0.633751967
NDC80	−1.4974775	7.142	−4.30164087	0.001131207	0.043046977	−0.630266987
AP1B1	1.11	8.429	4.28	0.001174262	0.043593147	−0.666022436
H2BFS	1.222	5.121	4.271	0.001191769	0.04384424	−0.68018847
MAP4K4	−1.04172561	7.215	−4.27171029	0.001191044	0.04384424	−0.679606089
PLD3	1.916	10.825	4.264	0.001208022	0.043913909	−0.693155632
ENPP1	−1.14642047	4.826	−4.26575893	0.00120333	0.043913909	−0.689430104
ITGA10	−1.85620797	7.214	−4.26030907	0.001214696	0.043913909	−0.69843019
IGKV1-37	1.831	7.021	4.236	0.001267234	0.044290054	−0.738968381
GPC6	−1.1298533	6.394	−4.23566454	0.001267508	0.044290054	−0.739175243
C9orf3	−1.47756582	6.871	−4.24153164	0.001254722	0.044290054	−0.729468257
GXYLT2	−1.69386575	5.555	−4.24355961	0.001250334	0.044290054	−0.726114027
VMO1	1.666	7.962	4.229	0.001281973	0.044349043	−0.750040061
MGARP	−1.55504243	5.353	−4.19551	0.001358735	0.045692391	−0.805723339
GLUL	1.145	11.202	4.182	0.001390136	0.046038611	−0.827601836
CD27	1.21	7.39	4.179	0.001399117	0.046139169	−0.833769133
MYLK	−1.14019221	6.013	−4.17280728	0.001413311	0.046410017	−0.843434981
LOC728061	−2.05163732	5.984	−4.16582764	0.001430544	0.04677797	−0.855041301
COL3A1	−2.07311618	10.754	−4.16094377	0.001442732	0.046974735	−0.86316603
SYNM	−2.20201792	7.297	−4.13903732	0.001498743	0.047474464	−0.899643872
IL4I1	1.077	7.981	4.13	0.001523648	0.047937254	−0.915428286
POR	1.289	7.363	4.114	0.001564286	0.048233071	−0.940638903
LURAP1L	−1.87326982	5.808	−4.11317906	0.001567777	0.048233071	−0.942774118
PEPD	1.135	8.808	4.105	0.00159094	0.048355035	−0.956822001
SYNC	−1.48850046	5.161	−4.10469247	0.001591146	0.048355035	−0.956946087
OMD	−2.78152739	5.449	−4.10474212	0.001591009	0.048355035	−0.956863151
PROCR	−1.00314734	7.544	−4.09518	0.001617771	0.048689939	−0.972840972
CD180	1.345	7.32	4.083	0.001653047	0.048855534	−0.993502199
PPFIBP1	−1.13010206	5.456	−4.07920891	0.001663519	0.048855534	−0.999550951
PRRX1	−1.6549019	6.099	−4.07511267	0.001675467	0.048855534	−1.0064061
CFH	−2.33548068	9.12	−4.07508164	0.001675558	0.048855534	−1.00645803
BGN	−1.62394918	8.095	−4.06341277	0.001710086	0.04915337	−1.02599645
COL15A1	−1.89798428	9.581	−4.06441292	0.001707098	0.04915337	−1.02432119
IGLL3P	2.172	9.334	4.06	0.001721112	0.049322321	−1.03215249
CYAT1	1.22	7.027	4.059	0.001723207	0.049322321	−1.03331779
ZNF404	−1.06352944	4.472	−4.05407513	0.001738248	0.049353524	−1.04164231
SFRP4	−2.93801794	6.929	−4.05424937	0.001737718	0.049353524	−1.04135026
IGLC1	1.596	7.517	4.046	0.001763359	0.049473158	−1.05538118
HLA-DMA	1.306	11.378	4.045	0.001765836	0.049473158	−1.05672574
CEP290	−1.0804849	6.391	−4.04268175	0.001773262	0.049621504	−1.0607457
CXCL3	1.317	7.891	4.039	0.001784045	0.049684365	−1.06655264
MS4A6E	1.668	4.81	4.037	0.001791087	0.049820889	−1.07032628
ACKR4	−1.52268155	4.42	−4.02988751	0.001813455	0.050044606	−1.0822148
EFEMP1	−1.54844572	8.354	−4.02769537	0.001820435	0.050157839	−1.08589504

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
LHFP	− 1.81885212	6.486	− 4.02237604	0.00183749	0.050516661	− 1.09482749
ADM	1.107	11.237	4.02	0.001845287	0.050543483	− 1.09888318
SEMA5A	− 1.41324129	6.863	− 4.01790982	0.001851938	0.050606592	− 1.10232973
C3orf80	− 1.72303094	4.81	− 4.01381707	0.001865281	0.050838319	− 1.10920649
ZNF667-AS1	− 1.74621215	6.251	− 3.99983639	0.001911615	0.051114758	− 1.13271066
PCDH10	− 2.08087587	5.158	− 4.00221063	0.001903663	0.051114758	− 1.12871765
CD52	1.832	10.092	3.997	0.001922413	0.051145657	− 1.13810607
TCN2	1.51	9.023	3.996	0.001924853	0.051145657	− 1.13932131
PILRA	1.096	8.679	3.99	0.001943711	0.051191763	− 1.14866009
RP11-182L21	− 1.17416448	6.41	− 3.98819442	0.001951108	0.051191763	− 1.15229877
METTL7B	2.348	7.441	3.974	0.00199995	0.05152927	− 1.17598256
HIST1H2BK	1.241	8.407	3.972	0.002006245	0.051555629	− 1.17899306
CALD1	− 1.15502391	6.474	− 3.97143398	0.002009454	0.051581145	− 1.18052373
MIR143HG	− 1.7863461	6.767	− 3.96581334	0.002029422	0.051859691	− 1.18999551
PTN	− 1.23570748	5.634	− 3.93877431	0.002128393	0.052998117	− 1.23560607
GJA1	− 1.84211055	9.798	− 3.93940584	0.002126025	0.052998117	− 1.23453994
SLITRK4	− 1.09949375	4.732	− 3.92826729	0.002168187	0.053248877	− 1.25334957
ZNF680	− 1.15108211	6.536	− 3.92920137	0.002164618	0.053248877	− 1.25177171
RP11-305O6	− 1.5668101	5.155	− 3.92047009	0.002198215	0.053590398	− 1.26652398
PEAR1	− 1.45350304	6.879	− 3.91007867	0.002238903	0.053945632	− 1.28409097
PCOLCE	− 1.46136398	8.89	− 3.90848164	0.002245225	0.053945632	− 1.28679173
SLIT2	− 1.73248051	7.539	− 3.91111181	0.002234823	0.053945632	− 1.28234394
MID1	− 1.21316819	6.613	− 3.90211625	0.002270606	0.054219745	− 1.29755876
OGN	− 3.53385479	5.648	− 3.90268222	0.002268337	0.054219745	− 1.29660127
NKG7	1.198	5.988	3.9	0.002277495	0.054328521	− 1.30046024
PHOSPHO2	− 1.27042123	5.769	− 3.89654933	0.002293047	0.054587647	− 1.30697841
CD72	1.917	7.487	3.881	0.002356347	0.055377521	− 1.33305954
TMEM133	− 1.46004818	4.868	− 3.88095243	0.002357148	0.055377521	− 1.3333853
SYTL2	− 1.07422641	5.833	− 3.87363677	0.00238785	0.055649564	− 1.34577929
FAIM3	1.669	7.098	3.868	0.002412198	0.055904268	− 1.35549554
IGLC1	1.244	5.63	3.865	0.002424514	0.055963427	− 1.36037311
COL16A1	− 1.47126191	7.34	− 3.85744434	0.002457281	0.056102143	− 1.37322983
PRORSD1P	− 1.25635926	5.119	− 3.8419094	0.002525854	0.056873241	− 1.39958844
CSPG4	− 1.70433251	6.435	− 3.83657651	0.002549847	0.05703302	− 1.40864197
C1QA	1.726	10.971	3.824	0.002607739	0.057988982	− 1.43014086
PCDH18	− 1.20010692	5.687	− 3.82245976	0.0026145	0.057988982	− 1.43262
SLC2A10	− 1.82473554	6.629	− 3.81256837	0.002660806	0.058145044	− 1.44943155
LOC101929787	− 1.52065348	6.235	− 3.79932411	0.002724138	0.058493484	− 1.47195507
ACP2	1.293	9.064	3.798	0.002728784	0.058500499	− 1.47358656
AC128677	1.314	7.689	3.796	0.002740529	0.058599953	− 1.47769888
CDH13	− 1.59536168	7.516	− 3.7881186	0.002778933	0.058710644	− 1.49102324
TM4SF1	− 1.13482268	6.372	− 3.78568638	0.002790976	0.05882372	− 1.49516351
SETBP1	− 2.04001615	5.492	− 3.78550728	0.002791865	0.05882372	− 1.49546841
AKR1B1	1.001	11.004	3.773	0.002855397	0.059250757	− 1.51701084
CD14	1.06	12.276	3.77	0.002869783	0.059352832	− 1.52182209

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
GM2A	1.026	8.328	3.763	0.00290519	0.059646061	−1.53356152
CHN1	−1.43327294	7.218	−3.75742871	0.002934899	0.060044226	−1.54330163
TGFBR3	−1.94883598	7.354	−3.75376994	0.002954086	0.060277845	−1.54953931
PKIG	−1.33129041	7.111	−3.75201347	0.002963342	0.060360921	−1.55253423
P2RX4	1.357	8.316	3.749	0.002977745	0.060495517	−1.55717564
LY86	1.05	10.429	3.741	0.003019884	0.060768315	−1.57062683
IGKC	1.131	6.415	3.737	0.003044466	0.060946901	−1.57838682
LINC00702	−1.44549954	5.255	−3.71950703	0.003140146	0.061821447	−1.60800455
FCER1G	1.055	10.016	3.71	0.003193331	0.061904366	−1.62407893
PLA2G7	1.197	11.348	3.709	0.003202244	0.061936817	−1.62674627
LINC00657	−1.36968121	8.481	−3.69566712	0.003276684	0.062315323	−1.64873798
COL5A1	−1.56308726	8.873	−3.69034404	0.003307996	0.062351143	−1.65783893
SDS	1.479	7.287	3.683	0.003350515	0.062655973	−1.67005981
TREM2	1.627	9.53	3.681	0.003364255	0.062761682	−1.67397568
RRN3P2	1.172	5.753	3.668	0.003442043	0.063601298	−1.69584691
COL6A3	−1.78321343	11.797	−3.6438087	0.003595174	0.064386793	−1.73748812
HBA1	2.739	8.398	3.641	0.003611872	0.064536915	−1.74192076
PTPN13	−1.03095065	4.503	−3.64078073	0.003614725	0.064538358	−1.74267599
HAMP	1.271	7.182	3.626	0.003709523	0.065529521	−1.76743745
AHNAK2	−1.16667494	7.662	−3.60878191	0.003828129	0.066019364	−1.79753723
CHSY3	−1.22204212	6.676	−3.60638586	0.00384462	0.066019364	−1.80164787
NR2F2	−1.52328366	5.648	−3.60405828	0.003860709	0.066019364	−1.80564141
NOV	−1.91939829	7.518	−3.61275996	0.00380091	0.066019364	−1.79071333
ADH1B	−2.23275369	5.263	−3.60611297	0.003846503	0.066019364	−1.80211607
KIAA1462	−1.23390712	5.005	−3.59957708	0.00389188	0.066123504	−1.81333093
CD200	−1.23990656	6.373	−3.59120956	0.003950777	0.066308294	−1.82769256
C11orf96	−1.8970491	9.023	−3.59326057	0.003936256	0.066308294	−1.82417191
NDP	−1.52712861	4.978	−3.58699312	0.0039808	0.066576401	−1.8349311
CCL23	1.185	4.999	3.578	0.004043445	0.066907955	−1.84985935
LOC100506585	1	6.671	3.573	0.00408413	0.067199089	−1.8594304
LOC100506558	−1.09670933	5.314	−3.57323447	0.004080407	0.067199089	−1.85855858
FMOD	−1.50776967	8.355	−3.57284018	0.004083299	0.067199089	−1.85923586
PCSK5	−1.28009798	6.504	−3.56713186	0.004125401	0.067544018	−1.86904207
UACA	−1.05013878	6.654	−3.55904856	0.004185783	0.068006558	−1.88293145
IGLV1-44	1.525	6.707	3.553	0.004232359	0.068367945	−1.89350824
IGK	2.096	8.425	3.548	0.004269896	0.068623023	−1.90194756
USP1	−1.14547526	7.686	−3.53669661	0.004357506	0.068950885	−1.92135753
AK025288	−1.98571356	8.033	−3.5350646	0.004370323	0.068982952	−1.92416424
GZMB	1.385	6.613	3.498	0.004675599	0.070549122	−1.9886731
CTSD	1.568	11.244	3.494	0.004708177	0.070735539	−1.99530536
LRRC15	−1.12921205	5.814	−3.48577685	0.004776139	0.071144001	−2.00899357
SLC9B2	−1.35623012	5.458	−3.48354936	0.004795364	0.071167995	−2.01283012
ADAM1A	−1.43593993	6.533	−3.47742566	0.004848625	0.071537196	−2.02337853
SLC22A18	1.314	8.866	3.476	0.00485765	0.071624955	−2.02515427
TPRA1	1.382	7.212	3.467	0.004939522	0.071966184	−2.04111418

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
PFN2	− 1.92215403	7.835	− 3.45452005	0.005053263	0.073210991	− 2.06284955
MT1M	− 1.20995452	5.25	− 3.45398354	0.00505816	0.073236371	− 2.06377435
PLAGL1	− 1.17697226	8.294	− 3.4374629	0.005211362	0.074103921	− 2.09225691
VGLL3	− 1.86051455	5.492	− 3.43570056	0.005227981	0.074103921	− 2.09529592
TGFB1I1	− 1.91203016	6.9	− 3.43770237	0.005209107	0.074103921	− 2.09184396
PBX1	− 1.01705906	5.355	− 3.43106813	0.005271926	0.074208576	− 2.1032848
FPR1	1.084	6.106	3.429	0.005290933	0.074385801	− 2.10671942
DDIT4	1.49	9.718	3.425	0.005334084	0.074579661	− 2.1144709
VCAN	− 1.5582745	9.014	− 3.42256774	0.005353546	0.074582358	− 2.11794629
TLCD2	− 1.01274834	5.575	− 3.41837151	0.005394312	0.074845274	− 2.12518497
COL24A1	− 1.20468207	5.625	− 3.41642392	0.00541334	0.074938028	− 2.12854486
FAM171A1	− 1.23232038	6.785	− 3.40813696	0.005495071	0.075042307	− 2.14284264
PDGFD	− 1.65623364	5.872	− 3.40000426	0.005576505	0.075615545	− 2.15687664
LOC101928916	− 1.24868866	9.412	− 3.38908463	0.005687782	0.075974146	− 2.17572328
abParts	1.055	6.89	3.378	0.005800963	0.076912316	− 2.19451488
TNFRSF11B	− 2.32614996	8.959	− 3.37306976	0.005855088	0.077249334	− 2.20337088
CCRL2	1.069	9.279	3.365	0.005937457	0.077894866	− 2.21669122
CCDC113	− 1.17122181	4.579	− 3.36082978	0.005986329	0.07824588	− 2.22450672
OLFML1	− 1.85943197	6.329	− 3.35750026	0.006022545	0.078508896	− 2.23025681
ZNF302	− 1.01985971	7.658	− 3.35151039	0.00608826	0.078859711	− 2.24060208
RUNDC3B	− 1.47075415	4.742	− 3.34993023	0.006105717	0.078867572	− 2.24333138
IGLL5	2.546	6.618	3.341	0.006207258	0.079187602	− 2.25905202
SAMSN1	1.212	6.716	3.3	0.006686271	0.082084201	− 2.32987484
RGS5	− 1.47176028	5.433	− 3.29976294	0.006687231	0.082084201	− 2.33001146
CCL18	1.7	12.378	3.297	0.006715839	0.082111048	− 2.33407705
PXDN	− 1.61084531	8.374	− 3.29718734	0.006718561	0.082111048	− 2.334463
PLK2	− 1.72107139	6.446	− 3.29524778	0.006742253	0.082290914	− 2.3378153
FCRL5	1.034	4.663	3.289	0.00681584	0.08239289	− 2.34815202
C12orf75	− 1.56631522	6.387	− 3.29035853	0.006802353	0.08239289	− 2.34626606
DHRS3	1.17	8.695	3.287	0.006843462	0.082497646	− 2.35200311
BACE2	− 1.13729452	8.3	− 3.2866389	0.00684844	0.082497646	− 2.35269546
DCN	− 1.27797183	6.941	− 3.27884117	0.006946086	0.082871272	− 2.36617454
PCDHB16	− 2.0403688	4.744	− 3.28141758	0.006913668	0.082871272	− 2.36172088
FPR3	1.108	8.998	3.275	0.006992625	0.082958974	− 2.37253155
FDX1	1.044	9.311	3.276	0.006982964	0.082958974	− 2.37121541
FBXL7	− 1.10298254	6.347	− 3.27704144	0.006968823	0.082958974	− 2.36928565
RP11-379H18	− 1.26161514	5.742	− 3.27700657	0.006969264	0.082958974	− 2.36934592
SDSL	1.193	7.509	3.272	0.007038201	0.083119231	− 2.37871581
HACE1	− 1.01249208	7.259	− 3.2716711	0.007037119	0.083119231	− 2.37856938
HLA-DMB	1	11.958	3.26	0.007185634	0.083941761	− 2.39844726
EPHX1	1.281	6.325	3.242	0.007430938	0.084942411	− 2.43038762
FNBP1L	− 1.17944856	7.479	− 3.2415762	0.007432599	0.084942411	− 2.43060032
TNC	− 1.37578741	7.69	− 3.23325442	0.007545881	0.085104671	− 2.44498911
AQP1	− 1.49341568	7.025	− 3.22534816	0.007655127	0.085609579	− 2.45865982
RP11-124L9	− 1.12643933	5.719	− 3.22277474	0.007691029	0.085757925	− 2.46310956

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
CXCL1	1.137	6.775	3.22	0.007727722	0.085890838	−2.46763557
SLC15A3	1.214	9.406	3.212	0.007839458	0.086081652	−2.48128533
HS3ST2	1.206	11.404	3.213	0.007834345	0.086081652	−2.480665
ANGPT1	−1.16253508	4.798	−3.19883173	0.008033349	0.08653032	−2.5045106
HBB	2.301	8.438	3.188	0.008200276	0.087217375	−2.52405622
LOC101928620	1.214	4.851	3.184	0.008254768	0.08769952	−2.53034954
LRRC49	−1.14867086	5.705	−3.17829006	0.008339302	0.088217178	−2.54002987
LAMA2	−1.0481289	5.445	−3.1670848	0.008511135	0.088660508	−2.55940451
ZNF423	−1.04457418	4.446	−3.16092116	0.008607175	0.089221833	−2.57006149
ZNF23	−1.11669749	7.011	−3.14224086	0.008904983	0.090230763	−2.60235781
LINC01279	−2.02681924	8.138	−3.14175538	0.00891286	0.090230763	−2.6031971
CTB-167B5	−2.31293162	5.307	−3.14420574	0.008873174	0.090230763	−2.5989609
FOLR2	1.192	7.817	3.138	0.008980412	0.090353121	−2.61036421
RAPGEF4	−1.03668555	4.378	−3.13513916	0.009020911	0.090543007	−2.6146349
LOC100127972	−1.01216172	5.313	−3.10834255	0.009472216	0.092466307	−2.66095306
COMP	−2.66774652	7.887	−3.10283885	0.009567691	0.092947345	−2.67046473
RP11-690I21	−1.02869854	6.001	−3.10092157	0.009601178	0.09298905	−2.67377809
SBDS	−1.11130408	6.895	−3.09837781	0.009645789	0.093140037	−2.678174
IL13RA2	−1.84607884	5.783	−3.08858504	0.009819488	0.093888012	−2.69509576
PLA2G15	1.04	9.387	3.086	0.009873995	0.094254348	−2.70034338
COL4A1	−1.59461938	9.74	−3.08497929	0.009884235	0.094301373	−2.70132592
MICU3	−1.65121416	4.776	−3.07900138	0.009992527	0.094778654	−2.71165409
MRGPRF	−1.32811473	6.587	−3.07627303	0.010042348	0.09500344	−2.71636764
SHISA3	−2.89115811	7.35	−3.07619179	0.010043835	0.09500344	−2.71650798
SCG5	−1.79294998	6.654	−3.07435902	0.010077448	0.095134323	−2.71967421
ESF1	−1.01991963	7.362	−3.07194815	0.010121835	0.09529178	−2.723839
C1QB	1.594	11.646	3.061	0.010327621	0.096081559	−2.74290853
PPAP2A	−1.18883309	8.397	−3.0473476	0.010586162	0.09748556	−2.76632741
LOXL1	−1.45575401	7.401	−3.04001176	0.010728726	0.09786511	−2.77899386
EFNB2	−1.7614713	6.572	−3.03366254	0.010853673	0.098363256	−2.78995536
MFAP5	−1.99102483	7.296	−3.01954597	0.011136735	0.099381171	−2.81432163
PRPF39	−1.08112002	7.339	−3.01372934	0.011255515	0.099836985	−2.82435944
HLA-DRA	1.05	12.472	3.008	0.011374911	0.100236116	−2.83434154
PALD1	−1.13409746	6.356	−3.00434742	0.011449785	0.100236116	−2.84054718
LIMS3-LOC440895	−1.00361209	4.943	−3.00361724	0.011465045	0.100236269	−2.8418069
SRGAP2C	−1.12202496	8.51	−2.99612123	0.01162289	0.100589895	−2.85473787
LILRB5	1.058	7.406	2.992	0.011711091	0.100834918	−2.861886
GUCY1B3	−1.09481873	6.043	−2.98824718	0.011791042	0.101074761	−2.86831842
MAP1B	−1.26295569	7.014	−2.98678584	0.011822517	0.10115834	−2.87083853
SLC14A1	−2.08714663	5.023	−2.97554416	0.012067475	0.102481695	−2.8902218
CAV1	−1.54266666	9.273	−2.97162638	0.012154033	0.102795272	−2.89697559
CAP2	−1.3285113	6.031	−2.97096325	0.012168746	0.10280373	−2.89811867
MCOLN1	1.463	8.13	2.969	0.01221883	0.102923357	−2.90199944
LUC7L3	−1.05672069	8.768	−2.96672843	0.012263123	0.103136633	−2.90541804
ZNF185	1.021	8.026	2.962	0.012375046	0.103527067	−2.91400079

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
GEM	− 1.31254579	9.126	− 2.94762008	0.012698168	0.104648883	− 2.9383431
G6PD	1.013	7.245	2.944	0.01278875	0.104955796	− 2.94505403
SMOC2	− 1.32742429	6.086	− 2.9416023	0.012838349	0.105122304	− 2.94870821
UHRF1	− 1.19022326	6.062	− 2.93775939	0.012928677	0.105337267	− 2.95532626
SMC3	− 1.25436837	6.196	− 2.93208304	0.013063263	0.105677166	− 2.96510026
ABHD17A	1.049	8.667	2.93	0.013104232	0.105861458	− 2.96805519
ANKRD36BP2	1.259	4.886	2.911	0.01358772	0.107455605	− 3.00223375
GOLGA8A	− 1.33502678	7.411	− 2.90660944	0.013684694	0.107892663	− 3.00893968
CCDC80	− 1.47135906	7.984	− 2.9019688	0.013801041	0.10811435	− 3.01692182
GPR124	− 1.04704431	6.619	− 2.90075678	0.013831591	0.108178391	− 3.01900633
GPRASP1	− 1.21408354	6.161	− 2.90013968	0.013847171	0.10821844	− 3.02006763
CSRP2	− 1.0528362	7.237	− 2.88943576	0.014120222	0.108979328	− 3.03847238
EDNRA	− 1.11557607	5.042	− 2.87552836	0.01448303	0.110117829	− 3.06237382
AJ420595	− 1.93827636	6.9	− 2.87065154	0.014612442	0.110360104	− 3.07075202
PCED1B	1.082	7.195	2.87	0.014631696	0.110385766	− 3.07199205
FLJ45482	− 1.15599542	5.962	− 2.86957912	0.014641055	0.110385766	− 3.07259417
TRIB2	− 1.33020834	6.242	− 2.86777486	0.014689318	0.110606956	− 3.07569325
SUSD5	− 1.7300781	4.347	− 2.86337332	0.014807725	0.110957286	− 3.08325256
CD300LF	1.196	8.828	2.858	0.014956045	0.111461795	− 3.09263505
RCAN2	− 2.3402395	7.039	− 2.85563237	0.015018278	0.111639705	− 3.09654358
COX7A1	− 1.12472813	7.883	− 2.85246805	0.015105203	0.111993538	− 3.10197535
ID4	− 1.25669749	5.511	− 2.84854904	0.015213555	0.112270462	− 3.10870155
BD495725	− 1.14536337	6.277	− 2.84711125	0.015253501	0.112454719	− 3.11116894
CYR61	− 1.64729732	9.399	− 2.8461505	0.015280251	0.11249641	− 3.11281758
MMP19	1.16	8.042	2.844	0.015336492	0.112556839	− 3.11627422
GCHFR	1.108	8.674	2.845	0.015325977	0.112556839	− 3.11562898
ACP5	1.066	11.566	2.842	0.015406513	0.112789619	− 3.12055977
MME	1.103	6.469	2.838	0.015503553	0.113203814	− 3.12646624
L3MBTL3	− 1.16706759	6.383	− 2.83821982	0.015502856	0.113203814	− 3.1264239
PSENEN	1.4	7.63	2.835	0.015600401	0.113510457	− 3.13232348
ADORA3	1.506	8.249	2.807	0.01639745	0.115441619	− 3.17916393
FHOD3	− 1.36684403	4.999	− 2.80469636	0.016480005	0.115626385	− 3.18388196
SYNPO2	− 1.04598587	5.51	− 2.80004775	0.01662025	0.116096583	− 3.19184194
IGLJ3	2.196	7.381	2.789	0.016943387	0.116649653	− 3.2099243
INTU	− 1.06120671	5.354	− 2.78933493	0.016947975	0.116649653	− 3.21017851
TTC14	− 1.02237882	7.064	− 2.78734066	0.017009688	0.116668823	− 3.21359085
SGCE	− 1.54727914	5.697	− 2.78702188	0.017019573	0.116668823	− 3.21413627
ALDH1A1	1.366	9.167	2.775	0.01740769	0.11764985	− 3.23529852
CWC27	− 1.03998318	7.371	− 2.77446547	0.017413512	0.11764985	− 3.23561225
PCDHB10	− 1.2483677	4.317	− 2.77218427	0.017486046	0.11771822	− 3.23951233
COL4A2	− 1.23543218	8.964	− 2.75287084	0.018112264	0.1194927	− 3.2725113
JAM2	− 1.57791951	5.778	− 2.75027808	0.018198006	0.119618316	− 3.27693846
MS4A4A	1.212	10.225	2.74	0.018540224	0.120631263	− 3.29439839
TNFSF4	− 1.3513573	5.39	− 2.73276259	0.018787856	0.121184544	− 3.30682809
GHR	− 1.27758998	4.535	− 2.71595095	0.019371777	0.122391782	− 3.33548585

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
GRAMD3	− 1.12266645	5.579	− 2.70354869	0.019814009	0.123078962	− 3.35660713
TMEM178A	− 1.10816793	4.327	− 2.68917108	0.020339164	0.124880621	− 3.38107034
LRRC32	− 1.29488862	7.886	− 2.68879414	0.020353115	0.124930459	− 3.38171138
BRE-AS1	1.21	5.413	2.68	0.020664605	0.125584268	− 3.39590751
CRYL1	1.018	9.3	2.673	0.020957562	0.126506082	− 3.40906024
LOC101930415	− 1.13138302	7.538	− 2.6697484	0.021070457	0.126805168	− 3.41407856
ITGA1	− 1.43419542	5.197	− 2.66572768	0.021225051	0.127197331	− 3.42090588
FHL2	− 1.36563838	8.325	− 2.65435513	0.021668391	0.128432655	− 3.44020578
LOC100134445	− 1.11977348	8.329	− 2.64334506	0.022106281	0.129903695	− 3.45887473
CYB561A3	1.151	9.832	2.642	0.02215034	0.129947681	− 3.46073208
SNORD50A	− 1.04346702	6.105	− 2.63943635	0.022263823	0.13022485	− 3.46549862
ZNF367	− 1.03406552	5.621	− 2.63477152	0.022453286	0.130646243	− 3.4734012
SCG2	− 2.46514311	5.894	− 2.62786288	0.022736797	0.131191602	− 3.48509962
PLN	− 1.77310428	4.955	− 2.62374641	0.022907396	0.131588944	− 3.49206697
LINC00622	− 1.29760971	4.816	− 2.62204858	0.022978124	0.131800122	− 3.49493996
CCDC3	− 1.14629604	8.171	− 2.61901746	0.02310493	0.131984439	− 3.50006811
BDP1	− 1.02156787	6.396	− 2.60396943	0.023744702	0.133564668	− 3.52550781
ATP6V0D2	1.299	7.947	2.603	0.023769522	0.133639702	− 3.52648047
CDC7	− 1.2299785	5.748	− 2.59773007	0.024015042	0.134500408	− 3.53604642
LOC100507311	− 1.1014119	4.723	− 2.59494021	0.024136896	0.134638546	− 3.54075683
C2orf40	− 2.00780375	5.604	− 2.58958986	0.024372284	0.134949872	− 3.54978718
EFEMP2	− 1.01495407	8.312	− 2.57717436	0.024927207	0.13607391	− 3.57072584
SGCG	− 1.23332282	5.997	− 2.57103843	0.02520601	0.136733928	− 3.58106551
EFHD1	− 1.39488703	6.468	− 2.57032983	0.025238403	0.136745109	− 3.58225919
KMO	1.092	8.409	2.57	0.02527123	0.136797207	− 3.58346726
IGFBP6	− 1.09339489	8.386	− 2.563997	0.025529721	0.137399954	− 3.59292392
HSPA2	− 1.16363559	6.492	− 2.5622374	0.025611248	0.137645677	− 3.59588606
INHBB	1.075	5.453	2.559	0.025760526	0.137945413	− 3.60128476
GYPC	1.031	8.17	2.558	0.025791692	0.13801015	− 3.60240783
RGS4	− 1.0175785	6.26	− 2.55787658	0.025814394	0.138036455	− 3.60322504
CADPS2	− 1.19152589	6.48	− 2.55757742	0.025828388	0.13807957	− 3.6037284
RARRES1	1.253	9.202	2.55	0.026188027	0.139012687	− 3.61656913
AQP9	1.41	9.605	2.545	0.026432749	0.139674824	− 3.62520339
LOC389834	− 1.2184531	7.174	− 2.54446388	0.026449147	0.139698017	− 3.62577899
TMEM45A	− 1.20152293	8.765	− 2.53745321	0.026786972	0.14073182	− 3.63755621
GPR183	1.037	9.969	2.533	0.026986459	0.141112074	− 3.64443905
LINC00619	− 1.0745705	3.743	− 2.52008766	0.027642021	0.14272822	− 3.6666939
SPRY4	− 1.15340389	7.363	− 2.51484388	0.027905412	0.143207217	− 3.67548254
FAM20A	1.074	7.481	2.514	0.027932064	0.143209492	− 3.67636706
PKIB	− 1.69038403	6.538	− 2.50121819	0.028601315	0.145050097	− 3.69829742
PPP1R14A	− 1.94935478	6.21	− 2.49821224	0.028757099	0.145327282	− 3.70332625
DNASE2B	1.139	6.444	2.486	0.029411775	0.146772313	− 3.72415661
VMP1	1.562	9.523	2.483	0.029580001	0.147133627	− 3.7294319
IGJ	3.104	8.864	2.482	0.029625818	0.147193406	− 3.73086328
PLOD2	− 1.16827633	8.908	− 2.47499807	0.029988334	0.14802969	− 3.74210872

(Cont. Supplementary Table 1)

	logFC	AveExpr	t	P.Value	adj.P.Val	B
LOC101927069	− 1.60316052	5.125	− 2.47180935	0.030161414	0.148104476	− 3.74742831
SPARCL1	− 1.88778385	9.426	− 2.47061628	0.030226422	0.148241776	− 3.74941817
GPX3	1.22	10.365	2.463	0.030651314	0.149356193	− 3.76231603
PRICKLE2	− 1.08501938	4.945	− 2.45977406	0.030823469	0.149757159	− 3.76748936
THBS1	− 1.00450902	6.406	− 2.45649882	0.031006068	0.150173348	− 3.77294402
PPP1R3C	− 1.10842436	5.881	− 2.45049465	0.031343543	0.15083513	− 3.78293825
CTGF	− 1.68043237	10.245	− 2.44316364	0.031760431	0.151849734	− 3.79513177
PLGLB1	− 1.04046038	5.02	− 2.44033293	0.031922839	0.152238333	− 3.79983726
ZNF521	− 1.25923381	4.897	− 2.43804712	0.032054572	0.152398313	− 3.80363583
PTPRZ1	− 1.04325	4.2	− 2.42396632	0.032877759	0.154295501	− 3.82701284
GPM6B	− 1.15925929	4.968	− 2.41770644	0.033250266	0.155136811	− 3.8373929
AK021977	− 1.05674346	5.415	− 2.40910828	0.033768584	0.156085006	− 3.85163739
OLFML2A	− 1.13887278	6.219	− 2.39552362	0.034603473	0.157597428	− 3.87411218
MANSC1	− 1.20061235	5.162	− 2.37742265	0.035746982	0.159649267	− 3.90399891
CX3CL1	− 1.20643257	6.702	− 2.37411628	0.035959764	0.160110005	− 3.90945057
MEOX1	− 1.3648004	5.619	− 2.37259553	0.036058041	0.160155144	− 3.91195724
FIGN	− 1.16179673	4.34	− 2.37020584	0.036212997	0.160409247	− 3.91589518
F3	− 1.2706323	7.831	− 2.36731755	0.036401141	0.160690719	− 3.9206531
AC012065	− 1.36960739	7.269	− 2.36455566	0.036581934	0.161096543	− 3.92520112
HSP90B1	− 1.0931333	6.992	− 2.35529786	0.037194283	0.162507108	− 3.94043371
FAM46C	1.128	6.681	2.331	0.038840666	0.164775579	− 3.98013075
DYSF	1.147	8.407	2.325	0.039302486	0.16534884	− 3.99095213
AKR1C3	− 1.37012153	8.401	− 2.3184279	0.039732384	0.166435652	− 4.00090724
LOC100506076	− 1.03285843	6.345	− 2.30883743	0.040419389	0.167696452	− 4.01658575
AK5	− 1.13886628	5.649	− 2.30470529	0.040718893	0.167998808	− 4.02333424
BC017398	− 1.18816092	4.847	− 2.29570776	0.041378431	0.169190839	− 4.03801454
SRGAP2B	− 1.49183273	7.338	− 2.28478755	0.042192668	0.170586274	− 4.05580544
LOC100130872	1.199	7.965	2.283	0.042330561	0.170715418	− 4.0587829
PDGFRB	− 1.21137854	7.133	− 2.26745861	0.043516326	0.172980554	− 4.08397666
CRYAB	− 1.00937569	7.311	− 2.26452563	0.043744255	0.173371994	− 4.08873726
IBSP	− 1.27075954	8.743	− 2.23484703	0.046115718	0.176965926	− 4.13678496
JPX	− 1.01960017	4.715	− 2.22531267	0.04690324	0.178402425	− 4.15217142
IFIT2	− 1.27238246	7.817	− 2.19997112	0.04905913	0.181687766	− 4.19294792