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Identification and interaction analysis of molecular markers in myocardial infarction by bioinformatics and next-generation sequencing data analysis

Basavaraj Vastrad¹ and Chanabasayya Vastrad^{2*} 

Abstract

Background Cardiovascular diseases are prevalent worldwide with any age, and it is characterized by sudden blockage of blood flow to heart and permanent damage to the heart muscle, whose cause and underlying molecular mechanisms are not fully understood. This investigation aimed to explore and identify essential genes and signaling pathways that contribute to the progression of MI.

Methods The aim of this investigation was to use bioinformatics and next-generation sequencing (NGS) data analysis to identify differentially expressed genes (DEGs) with diagnostic and therapeutic potential in MI. NGS dataset (GSE132143) was downloaded from the Gene Expression Omnibus (GEO) database. DEGs between MI and normal control samples were identified using the DESeq2 R bioconductor tool. The gene ontology (GO) and REACTOME pathway enrichment analyses of the DEGs were performed using g:Profiler. Next, four kinds of algorithms in the protein–protein interaction (PPI) were performed to identify potential novel biomarkers. Next, miRNA-hub gene regulatory network analysis and TF-hub gene regulatory network were constructed by miRNet and NetworkAnalyst database, and Cytoscape software. Finally, the diagnostic effectiveness of hub genes was predicted by receiver operator characteristic curve (ROC) analysis and AUC more than 0.800 was considered as having the capability to diagnose MI with excellent specificity and sensitivity.

Results A total of 958 DEGs were identified, consisting of 480 up-regulated genes and 478 down-regulated genes. The enriched GO terms and pathways of the DEGs include immune system, neuronal system, response to stimulus and multicellular organismal process. Ten hub genes (namely *cfr*, *cdk1*, *rps13*, *rps15a*, *rps27*, *notch1*, *mrpl12*, *nos2*, *ccdc85b* and *atn1*) were obtained via protein–protein interaction analysis results. MiRNA-hub gene regulatory network and TF-hub gene regulatory network showed that *hsa-mir-409-3p*, *hsa-mir-3200-3p*, *creb1* and *tp63* might play an important role in the MI.

Conclusions Analysis of next-generation sequencing dataset combined with global network information and validation presents a successful approach to uncover the risk hub genes and prognostic markers of MI. Our investigation identified four risk- and prognostic-related gene signatures, including *cfr*, *cdk1*, *rps13*, *rps15a*, *rps27*, *notch1*, *mrpl12*, *nos2*, *ccdc85b* and *atn1*. This gene sets contribute a new perspective to improve the diagnostic, prognostic, and therapeutic outcomes of MI.

Keywords Bioinformatics, Biomarkers, Myocardial infarction, Next-generation sequencing, Pathways

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Background

Myocardial infarction (MI) is one of the most commonly diagnosed cardiovascular diseases prevalent worldwide [1]. The clinical prevalence of MI is approximately 18 million people worldwide [1], and its main features such as the presence of sudden blockage of blood flow to heart and permanent damage to the heart muscle [2]. MI becomes the chief cause of morbidity and mortality all over the world [3]. Studies have revealed that the progression of MI is related to genetic factors [4], older age [5], smoking [6], hypertension [7], diabetes mellitus [8] and obesity [9]. However, the molecular pathogenesis of MI has not been explored comprehensively. In current years, molecular biomarkers were demonstrated highly useful as clinical tools for MI diagnosis [10, 11]. A key molecular target for diagnosis and reexamination is essential for therapeutic action and prognostic outcome of MI patients.

The diagnosis of MI, however, remains a challenge due to the complex clinical features and the lack of definitive diagnostic tests or biomarkers in the early stages. Several studies have described that significant molecular biomarkers in MI were identified as prognostic or therapeutic factors such as *hmg1* [12], *stxbp2* [13], *ccl19* and *ccl21* [14], *nlrp3* [15] and *cd14* [16]. Molecular biology investigation has identified numerous signaling pathways that contribute to the progression of MI, including, Nrf2/HO-1; TLR4/TNF- α signaling pathway [17], Wnt/ β -catenin signaling pathway [18], β 2AR, cAMP/PKA, and BDNF/TrkB signaling pathways [19], PTEN/PI3K/Akt signaling pathway [20] and TGF- β 1/SMAD2 signaling pathway [21]. It is very essential to explore the molecular characteristics and mechanism of MI occurrence, advancement to contribute novel approach for the effective prevention, diagnosis and treatment of MI.

In current investigation, next-generation sequencing (NGS) technology based on high-throughput platforms has been extensively used to scrutinize and determine the encouraging biomarkers for diagnosis and prognosis of disease at the genome level. With the wide application of bioinformatics and NGS data analysis, a huge number of cores data have been produced, and most of the NGS data have been deposited and stored in public database Gene Expression Omnibus (GEO) database (<http://www.ncbi.nlm.nih.gov/geo/>) [24]. Bioinformatics and NGS data analysis have been carried out on cardiovascular diseases in recently years [22], and hundreds of differentially expressed genes (DEGs) have been obtained. In perspective of this, the plan of this investigation is to analyze NGS data related to the pathogenesis of MI from the public database, which provide novel understanding into the molecular mechanisms of MI.

Here, we analyzed the MI NGS dataset GSE132143 [23] was downloaded from the GEO database and performed the identification of differentially expressed genes (DEGs) between the MI samples and normal control samples. Afterward, gene ontology (GO) terms and REACTOME pathways linked with DEGs were marked to illuminate the gene enrichment in MI. A protein–protein interaction network (PPIN) was generated to resolve the hub genes linked with MI. Moreover, miRNA-hub gene regulatory network analysis and TF-hub gene regulatory network, and the miRNA and TFs were identified according to degree parameters. Finally, hub genes were validated via receiver operating characteristic curve (ROC) analysis. In brief, these outcomes determined that the most genes might have probable value in prognosis and diagnosis of MI.

Methods

Data resources

The GEO database is a national depository of genetic information databases of next-generation sequencing data. In this investigation, we retrieved NGS dataset GSE132143 [23] from the GEO database. GSE132143 (Platform GPL18573 Illumina NextSeq 500 (Homo sapiens)) comprised 20 MI samples and 12 normal control samples.

Identification of DEGs

DESeq2 of R/Bioconductor software package [25] was accessible to determine the DEGs between MI and normal control samples. The log-fold change (FC) and adjusted *P*-values (adj. *P*) were resolved. The adj. *P* using the Benjamini–Hochberg method with default values was enforced to accurate the probable false-positive results [26]. According standard statistical protocol or literature ($\log_{2}FC > 1$ and $\log_{2}FC < -1$) and $\text{adj. } p\text{-Val} < 0.05$ are significant up- and down-regulated genes selection. Genes that met the definite cut-off criteria of $\text{adj. } P < 0.05$ and $|\log_{2}FC| > 1.37$ were marked as up-regulated DEGs and $|\log_{2}FC| < -1.89$ was marked as down-regulated DEGs. We used a ggplot2 and gplot package of R/Bioconductor software to generate volcano plots and heatmap of the DEGs.

GO and REACTOME pathway enrichment analysis of DEGs

The DEGs with the strongest associations were selected for GO and REACTOME pathway enrichment analysis. Moreover, GO and REACTOME pathway enrichment analysis were used to further determine the potential functions of the essential genes associated in MI. To effectively examine the biological content behind DEGs, the g:Profiler (<http://biit.cs.ut.ee/gprofiler/>) [29] was used to gain the set of functional annotation. GO enrichment

analysis (GO, <http://www.geneontology.org>) [27] is a broadly used tool for annotating genes with probable functions, such as biological process (BP), cellular component (CC), and molecular function (MF). REACTOME (<https://reactome.org/>) [28] pathway enrichment analysis is an efficient resource for analytical investigation of gene functions and linked high-level genome functional information. $p < 0.05$ was marked as the threshold value.

Construction of the PPI network and module analysis

The Human Integrated Protein–Protein Interaction rEference (HIPPIE) (<http://cbdm-01.zdv.uni-mainz.de/~mschaefer/hippie/>) [30] database is an online search tool used to analyze accepted proteins and predict PPI networks, including direct and indirect interactions between proteins and their functional correlations and then software Cytoscape (version 3.8.2) (<http://www.cytoscape.org/>) [31] was engaged to accommodate and visualize PPI networks. HIPPIE is an experimentally validated PPI database. PPI networks can advance the examination of molecular targets, signaling pathways, and network functions associated in the advancement of MI. Hub genes are associated biological processes and diseases progression. Subsequently, we utilized a plug-in Network Analyzer of Cytoscape to resolve hub genes according to the algorithms, including node degree [32], betweenness centrality [33], stress centrality [34] and closeness centrality [35]. The PEWCC1 [36] plug-in was used to cover the hub gene modules in the PPI network.

MiRNA-hub gene regulatory network construction

MicroRNAs can inflect hub gene expression by promoting or inhibiting mRNA degradation and translation. Target hub gene information of miRNAs was collected from miRNet database (<https://www.mirnet.ca/>) [37], which is an experimentally validated miRNA-hub gene interactions database. The intersection of target hub genes of miRNAs in MI was used to construct the miRNA-hub gene-regulated network. The miRNA-hub gene regulatory network of the hub genes and their targeted miRNAs was visualized by Cytoscape software [31].

TF-hub gene regulatory network construction

Transcription factors (TFs) can inflect hub gene expression by promoting mRNA translation. Target hub gene information of TFs was collected from NetworkAnalyst database (<https://www.networkanalyst.ca/>) [38], which is an experimentally validated TF-hub gene interactions database. The intersection of target hub genes of TFs in MI was used to construct the TF-hub gene-regulated network. The TF-hub gene regulatory network of the hub genes and their targeted TFs was visualized by Cytoscape software [31].

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

The linear discriminant analysis (LDA) with combined selected hub genes was used to identify biomarkers with high sensitivity and specificity for MI diagnosis. Here, we used one data as training dataset and other data as validation dataset iteratively. The receiver operator characteristic curves were plotted, and area under curve (AUC) was determined separately to check the achievement of LDA model using the R packages “pROC” [39]. A $AUC > 0.8$ determined that the model had a favorable fitting effect.

Results

Identification of DEGs

In our investigation, 958 DEGs were identified between MI samples and normal control samples. Among them, 480 were up-regulated genes ($|\log_{2}FC| > 1.37$) and 478 were down-regulated genes ($|\log_{2}FC| < -1.89$) (Table 1). The volcano plot (Fig. 1) was used to show the expression pattern of DEGs in MI (volcano plots presented the distributions of differentially expressed genes; Green dots—up-regulated genes and red dots—down-regulated genes). The heatmap of the DEGs (heat maps explains the gene expression levels in dataset) is shown in Fig. 2.

GO and REACTOME pathway enrichment analysis of DEGs

A total of 480 up-regulated genes and 478 down-regulated genes were analyzed by g:Profiler software. GO enrichment analysis covers three aspects: BP, CC and MF (Table 2). The up-regulated genes were mainly related to response to stimulus, cell communication, cell periphery, membrane, molecular transducer activity and transmembrane signaling receptor activity; while the down-regulated genes were mainly involved in multicellular organismal process, anatomical structure development, cell periphery, plasma membrane, inorganic molecular entity transmembrane transporter activity and structural molecule activity. Moreover, REACTOME pathway enrichment analysis indicated that the up-regulated genes were involved in immune system and innate immune system, while down-regulated genes were involved in neuronal system and extracellular matrix organization (Table 3).

Construction of the PPI network and module analysis

Considering the critical role of protein interactions in protein function, we used the HIPPIE database and Cytoscape software to generate PPI network once we had identified the 958 DEGs. The results showed that there were dense regions in PPI, that is, genes closely related to MI. A total of 6292 nodes and 12,582 edges were selected to plot the PPI network (Fig. 3). The Network Analyzer plugin of Cytoscape was used to score each nodes by 4

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

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
RNY4	5.579746	5.51E-29	1.24E-25	11.17324	Up	RNA, Ro60-associated Y4
UMODL1-AS1	4.641232	0.001219	0.00548	3.234363	Up	UMODL1 antisense RNA 1
IL1RL1	4.151538	1.75E-58	3.14E-54	16.12332	Up	interleukin 1 receptor like 1
ANKRD22	4.141446	3.01E-07	5.69E-06	5.122728	Up	ankyrin repeat domain 22
RNF17	4.108169	0.000161	0.001042	3.773882	Up	ring finger protein 17
SERPINA3	3.927298	3.29E-25	4.38E-22	10.37301	Up	serpin family A member 3
ALOX15B	3.835862	1.18E-09	5.17E-08	6.083183	Up	arachidonate 15-lipoxygenase type B
RNASE2	3.752758	2.22E-18	9.86E-16	8.745419	Up	ribonuclease A family member 2
SCGN	3.723034	2.93E-13	3.81E-11	7.297616	Up	secretagoin, EF-hand calcium binding protein
CD177	3.636629	3.07E-09	1.16E-07	5.927867	Up	CD177 molecule
AOX1	3.346982	2.05E-29	5.27E-26	11.26066	Up	aldehyde oxidase 1
TUBA3C	3.255294	2.00E-24	2.32E-21	10.19912	Up	tubulin alpha 3c
RNA5SP304	3.253096	0.00245	0.009651	3.029451	Up	RNA, 5S ribosomal pseudogene 304
VSIG4	3.210108	4.37E-43	2.62E-39	13.76103	Up	V-set and immunoglobulin domain containing 4
OR4M2	3.18715	0.000186	0.001175	3.737391	Up	olfactory receptor family 4 subfamily M member 2
PLA2G2A	3.173675	1.37E-10	8.44E-09	6.419057	Up	phospholipase A2 group IIA
S100A9	3.165379	5.96E-20	3.63E-17	9.145122	Up	S100 calcium binding protein A9
CLECL1	3.110064	8.15E-06	8.95E-05	4.461245	Up	C-type lectin like 1
RNU7-154P	3.097763	2.53E-06	3.39E-05	4.705354	Up	RNA, U7 small nuclear 154 pseudogene
OR11J1P	3.076974	0.001508	0.006505	3.173052	Up	olfactory receptor family 11 subfamily J member 1 pseudogene
KRT5	3.053882	4.29E-07	7.59E-06	5.055631	Up	keratin 5
ADORA3	3.038127	1.92E-22	1.64E-19	9.745705	Up	adenosine A3 receptor
VTRNA1-3	2.994675	5.45E-05	0.000426	4.035285	Up	vault RNA 1-3
IL1R2	2.966613	1.77E-20	1.15E-17	9.275601	Up	interleukin 1 receptor type 2
SLC22A16	2.965856	9.98E-07	1.54E-05	4.892085	Up	solute carrier family 22 member 16
LCN6	2.962512	6.60E-13	7.98E-11	7.187499	Up	lipocalin 6
OR11J6P	2.921939	0.002486	0.009764	3.025091	Up	olfactory receptor family 11 subfamily J member 6 pseudogene
FPR1	2.899739	3.40E-23	3.22E-20	9.920097	Up	formyl peptide receptor 1
CCL20	2.880525	0.002778	0.010673	2.991299	Up	C-C motif chemokine ligand 20
OR11J5P	2.873974	0.006063	0.020166	2.744378	Up	olfactory receptor family 11 subfamily J member 5 pseudogene
FCGBP	2.833765	2.44E-10	1.36E-08	6.330939	Up	Fc fragment of IgG binding protein
TUBA3D	2.826436	8.97E-19	4.19E-16	8.847233	Up	tubulin alpha 3d
DEFB1	2.824242	0.006277	0.020749	2.732965	Up	defensin beta 1
MT1A	2.794836	4.32E-06	5.27E-05	4.595148	Up	metallothionein 1A
LYVE1	2.765871	2.58E-18	1.10E-15	8.728434	Up	lymphatic vessel endothelial hyaluronan receptor 1
CD163	2.752851	6.32E-23	5.68E-20	9.858199	Up	CD163 molecule
S100A8	2.74215	2.04E-13	2.74E-11	7.346254	Up	S100 calcium binding protein A8
MCEMP1	2.716497	1.26E-05	0.000128	4.367627	Up	mast cell expressed membrane protein 1
SNORA63C	2.710838	4.23E-09	1.50E-07	5.875085	Up	small nucleolar RNA, H/ACA box 63C
ADAMDEC1	2.706414	0.000105	0.000735	3.878508	Up	ADAM like decysin 1
OR52N5	2.697679	6.10E-05	0.000467	4.009009	Up	olfactory receptor family 52 subfamily N member 5
S100A12	2.691859	8.03E-07	1.29E-05	4.934546	Up	S100 calcium binding protein A12
CEP55	2.677728	2.15E-12	2.22E-10	7.024705	Up	centrosomal protein 55
TSIX	2.677281	0.001517	0.006534	3.171444	Up	TSIX transcript, XIST antisense RNA
PRR32	2.672892	0.00014	0.000932	3.807299	Up	proline rich 32
TUBAP8	2.646856	8.22E-18	3.21E-15	8.596545	Up	tubulin alpha pseudogene 8

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
RARRES1	2.639969	3.51E-15	7.50E-13	7.871404	Up	retinoic acid receptor responder 1
PPEF1	2.634499	4.14E-08	1.06E-06	5.48478	Up	protein phosphatase with EF-hand domain 1
TUBA3E	2.62609	1.34E-16	3.88E-14	8.270167	Up	tubulin alpha 3e
MMRN1	2.609449	4.57E-07	8.01E-06	5.043397	Up	multimerin 1
TUBAP9	2.607613	3.60E-16	9.81E-14	8.151167	Up	tubulin alpha pseudogene 9
IGLV8-61	2.601016	0.002496	0.009796	3.023796	Up	immunoglobulin lambda variable 8-61
FAM83B	2.59668	1.40E-05	0.000139	4.344196	Up	family with sequence similarity 83 member B
MTRNR2L11	2.594186	3.90E-06	4.85E-05	4.616414	Up	MT-RNR2 like 11
CHI3L2	2.586472	2.91E-08	7.87E-07	5.546483	Up	chitinase 3 like 2
TLR2	2.575405	3.82E-26	6.53E-23	10.57685	Up	toll-like receptor 2
EDN2	2.563355	5.73E-06	6.68E-05	4.536064	Up	endothelin 2
DAW1	2.553361	3.73E-05	0.000315	4.123305	Up	dynein assembly factor with WD repeats 1
VN1R60P	2.54999	0.000364	0.002036	3.565248	Up	vomer nasal 1 receptor 60 pseudogene
RNVU1-34	2.511083	0.005435	0.01846	2.78008	Up	RNA, variant U1 small nuclear 34
PTPRQ	2.479308	8.65E-07	1.37E-05	4.919996	Up	protein tyrosine phosphatase receptor type Q
RNY1	2.473187	6.23E-21	4.39E-18	9.386102	Up	RNA, Ro60-associated Y1
DMP1	2.471165	4.32E-05	0.000355	4.089639	Up	dentin matrix acidic phosphoprotein 1
NPTX2	2.470985	9.88E-15	1.93E-12	7.740761	Up	neuronal pentraxin 2
SCARNA23	2.461822	3.28E-06	4.21E-05	4.652554	Up	small Cajal body-specific RNA 23
ADH1B	2.434671	1.06E-13	1.55E-11	7.432747	Up	alcohol dehydrogenase 1B (class I), beta polypeptide
BANCR	2.426012	0.002137	0.008615	3.070478	Up	BRAF-activated non-protein coding RNA
SLC25A48	2.417088	0.001385	0.006079	3.19779	Up	solute carrier family 25 member 48
HAS2	2.41656	4.24E-12	4.08E-10	6.928801	Up	hyaluronan synthase 2
CYP4B1	2.412669	4.86E-08	1.22E-06	5.456384	Up	cytochrome P450 family 4 subfamily B member 1
PTX3	2.409897	5.51E-08	1.35E-06	5.433987	Up	pentraxin 3
TMIGD3	2.389688	9.50E-14	1.40E-11	7.447722	Up	transmembrane and immunoglobulin domain containing 3
IGLV5-45	2.388431	0.01611	0.044452	2.406423	Up	immunoglobulin lambda variable 5-45
FCGR1CP	2.386298	1.82E-08	5.25E-07	5.628699	Up	Fc fragment of IgG receptor 1c, pseudogene
CYP4Z2P	2.378179	2.24E-10	1.27E-08	6.343886	Up	cytochrome P450 family 4 subfamily Z member 2, pseudogene
TIMP4	2.371008	1.14E-21	8.91E-19	9.563326	Up	TIMP metalloproteinase inhibitor 4
CLEC4D	2.362952	6.35E-06	7.27E-05	4.514519	Up	C-type lectin domain family 4 member D
PKHD1	2.362583	0.000394	0.002175	3.544286	Up	PKHD1 ciliary IPT domain containing fibrocystin/polyductin
LCN15	2.361396	3.07E-06	3.98E-05	4.666394	Up	lipocalin 15
TBX22	2.356449	4.39E-06	5.33E-05	4.591911	Up	T-box transcription factor 22
MT1X	2.355976	7.70E-11	5.15E-09	6.506265	Up	metallothionein 1X
AREG	2.349214	7.74E-07	1.25E-05	4.941783	Up	amphiregulin
MTRNR2L1	2.315705	1.79E-05	0.00017	4.289007	Up	MT-RNR2 like 1
BMP3	2.284982	0.00529	0.018076	2.788837	Up	bone morphogenetic protein 3
FCGR1A	2.283693	1.24E-07	2.69E-06	5.286831	Up	Fc fragment of IgG receptor 1a
CYP4Z1	2.28039	2.63E-15	5.69E-13	7.907311	Up	cytochrome P450 family 4 subfamily Z member 1
SCARNA18	2.279144	4.16E-06	5.10E-05	4.603175	Up	small Cajal body-specific RNA 18
IGKV1D-8	2.277938	0.004821	0.01679	2.818735	Up	immunoglobulin kappa variable 1D-8
EDNRB	2.27515	1.09E-24	1.36E-21	10.25763	Up	endothelin receptor type B
HOPX	2.274613	5.56E-06	6.51E-05	4.542481	Up	HOP homeobox
SLC19A2	2.272137	2.31E-28	4.89E-25	11.04517	Up	solute carrier family 19 member 2
FGF10	2.268452	1.34E-05	0.000135	4.352848	Up	fibroblast growth factor 10

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
RNU6ATAC	2.267968	9.60E-12	8.42E-10	6.812355	Up	RNA, U6atac small nuclear (U12-dependent splicing)
SULT1B1	2.265755	1.88E-29	5.21E-26	11.26816	Up	sulfotransferase family 1B member 1
RNF175	2.241455	6.52E-13	7.97E-11	7.189055	Up	ring finger protein 175
METTL7B	2.241047	6.64E-13	8.00E-11	7.186735	Up	methyltransferase like 7B
SLC66A1L	2.238488	2.75E-08	7.53E-07	5.556597	Up	solute carrier family 66 member 1 like
RHAG	2.234748	1.76E-09	7.24E-08	6.018624	Up	Rh-associated glycoprotein
BBS12	2.22376	7.34E-19	3.57E-16	8.869598	Up	Bardet-Biedl syndrome 12
NAA11	2.22176	1.49E-10	9.01E-09	6.406717	Up	N-alpha-acetyltransferase 11, NatA catalytic subunit
SIGLEC10	2.22094	1.26E-13	1.81E-11	7.41021	Up	sialic acid binding Ig like lectin 10
MUC16	2.216738	0.014897	0.041734	2.434877	Up	mucin 16, cell surface associated
PGA3	2.215169	1.41E-10	8.65E-09	6.414678	Up	pepsinogen A3
PSMC6P2	2.21118	0.00139	0.006096	3.196821	Up	proteasome 26S subunit, ATPase, 6 pseudogene 2
SYT13	2.208971	2.18E-10	1.24E-08	6.348444	Up	synaptotagmin 13
GCKR	2.208122	0.017034	0.046402	2.385967	Up	glucokinase regulator
BLM	2.202519	7.80E-15	1.58E-12	7.77072	Up	BLM RecQ like helicase
CLEC4E	2.201741	1.54E-08	4.58E-07	5.657125	Up	C-type lectin domain family 4 member E
SNORA79B	2.198363	8.76E-09	2.80E-07	5.753229	Up	small nucleolar RNA, H/ACA box 79B
CCL23	2.197519	0.005056	0.017437	2.803422	Up	C-C motif chemokine ligand 23
LILRA5	2.193247	3.83E-13	4.86E-11	7.26143	Up	leukocyte immunoglobulin like receptor A5
OR13A1	2.192713	0.005946	0.019856	2.750736	Up	olfactory receptor family 13 subfamily A member 1
OLAH	2.19267	0.000509	0.002675	3.475758	Up	oleoyl-ACP hydrolase
FAM111B	2.190301	3.70E-09	1.35E-07	5.897066	Up	family with sequence similarity 111 member B
H1-3	2.182279	2.34E-11	1.83E-09	6.682796	Up	H1.3 linker histone, cluster member
MGST1	2.180525	5.20E-12	4.89E-10	6.900083	Up	microsomal glutathione S-transferase 1
SERPINA5	2.175708	1.29E-10	8.02E-09	6.428188	Up	serpin family A member 5
PGA4	2.169584	2.23E-08	6.27E-07	5.593241	Up	pepsinogen A4
SLCO4A1	2.164331	2.12E-09	8.46E-08	5.988367	Up	solute carrier organic anion transporter family member 4A1
WNK3	2.160356	2.36E-17	8.15E-15	8.474641	Up	WNK lysine deficient protein kinase 3
RNU6-509P	2.159622	0.015302	0.042636	2.425163	Up	RNA, U6 small nuclear 509, pseudogene
CAMP	2.145519	0.001607	0.006843	3.154709	Up	cathelicidin antimicrobial peptide
KAZN-AS1	2.142912	2.21E-07	4.38E-06	5.180542	Up	KAZN antisense RNA 1
SPP1	2.13936	1.59E-11	1.30E-09	6.739139	Up	secreted phosphoprotein 1
CYP4A11	2.139264	1.81E-09	7.41E-08	6.013846	Up	cytochrome P450 family 4 subfamily A member 11
SLC11A1	2.136032	3.58E-11	2.64E-09	6.620698	Up	solute carrier family 11 member 1
LBP	2.135988	0.004083	0.014678	2.871715	Up	lipopolysaccharide binding protein
IL18R1	2.129729	4.99E-27	8.97E-24	10.76585	Up	interleukin 18 receptor 1
ALOX5AP	2.129693	2.56E-19	1.42E-16	8.986085	Up	arachidonate 5-lipoxygenase activating protein
DLGAP5	2.126079	8.58E-09	2.75E-07	5.756689	Up	DLG-associated protein 5
TRPM1	2.118343	0.005435	0.018461	2.780023	Up	transient receptor potential cation channel subfamily M member 1
PGA5	2.105342	3.17E-08	8.38E-07	5.53197	Up	pepsinogen A5
MS4A4A	2.10156	5.21E-13	6.50E-11	7.219725	Up	membrane spanning 4-domains A4A
SCN10A	2.093768	1.60E-05	0.000155	4.314862	Up	sodium voltage-gated channel alpha subunit 10
RPS15AP17	2.093492	3.06E-08	8.17E-07	5.538211	Up	ribosomal protein S15a pseudogene 17
H3C7	2.092387	5.52E-09	1.88E-07	5.830827	Up	H3 clustered histone 7
SPINK1	2.092288	0.00248	0.009746	3.025777	Up	serine peptidase inhibitor Kazal type 1

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
RETN	2.091833	0.006533	0.021451	2.719762	Up	resistin
KNG1	2.090394	0.000456	0.002439	3.50563	Up	kininogen 1
CCR1	2.089325	1.64E-16	4.66E-14	8.246202	Up	C-C motif chemokine receptor 1
RNU5A-1	2.088339	3.86E-09	1.39E-07	5.890004	Up	RNA, U5A small nuclear 1
CSTA	2.085995	1.34E-08	4.07E-07	5.680351	Up	cystatin A
AKR1B10	2.083723	0.002081	0.008428	3.078414	Up	aldo-ketoreductase family 1 member B10
LCN10	2.082085	9.14E-05	0.000656	3.912387	Up	lipocalin 10
EEF1A1P31	2.077653	5.27E-16	1.39E-13	8.10499	Up	eukaryotic translation elongation factor 1 alpha 1 pseudogene 31
NMRAL2P	2.076921	4.54E-05	0.000368	4.078135	Up	NmrA like redox sensor 2, pseudogene
VN1R28P	2.072231	0.003277	0.012218	2.940453	Up	vomer nasal 1 receptor 28 pseudogene
IGKV2D-40	2.071097	0.016582	0.045462	2.395849	Up	immunoglobulin kappa variable 2D-40
SLA	2.070975	5.49E-16	1.43E-13	8.100123	Up	Src like adaptor
MYOT	2.064989	3.34E-09	1.24E-07	5.913712	Up	myotilin
BEND2	2.062686	8.83E-05	0.000637	3.920554	Up	BEN domain containing 2
RN7SL191P	2.061233	0.003769	0.013734	2.896892	Up	RNA, 7SL, cytoplasmic 191, pseudogene
GRM7-AS3	2.059395	0.008743	0.027172	2.621958	Up	GRM7 antisense RNA 3
RN7SKP94	2.058874	6.22E-05	0.000475	4.004117	Up	RN7SK pseudogene 94
ADH1A	2.056145	7.65E-10	3.62E-08	6.152026	Up	alcohol dehydrogenase 1A (class I), alpha polypeptide
GALNTL6	2.037105	1.22E-05	0.000124	4.374844	Up	polypeptide N-acetylgalactosaminyltransferase like 6
CYP4A22	2.032709	2.98E-10	1.61E-08	6.300046	Up	cytochrome P450 family 4 subfamily A member 22
CYP4A27P	2.02855	0.000406	0.002231	3.535845	Up	cytochrome P450 family 4 subfamily A member 27, pseudogene
TLR8	2.026412	1.80E-10	1.06E-08	6.377081	Up	toll-like receptor 8
FCGR3A	2.018412	1.05E-09	4.70E-08	6.101938	Up	Fc fragment of IgG receptor IIIa
PKHD1L1	2.015925	0.000719	0.003562	3.38222	Up	PKHD1 like 1
SIGLEC12	2.011093	0.003131	0.011755	2.954528	Up	sialic acid binding Ig like lectin 12
TAS2R7	2.00703	2.95E-05	0.000259	4.177281	Up	taste 2 receptor member 7
SHISA3	1.999131	8.92E-11	5.73E-09	6.484225	Up	shisa family member 3
F13A1	1.993279	3.46E-14	5.58E-12	7.579783	Up	coagulation factor XIII A chain
RPS8P10	1.992515	9.08E-05	0.000653	3.913873	Up	ribosomal protein S8 pseudogene 10
CDH19	1.991141	6.48E-08	1.56E-06	5.40494	Up	cadherin 19
H4C13	1.989227	3.22E-06	4.15E-05	4.656473	Up	H4 clustered histone 13
FCGR1B	1.979038	3.17E-07	5.93E-06	5.113214	Up	Fc fragment of IgG receptor Ib
EPCAM	1.977482	0.003209	0.011992	2.946991	Up	epithelial cell adhesion molecule
ZDHHC20P1	1.977408	0.016427	0.045168	2.399297	Up	zinc finger DHHC-type containing 20 pseudogene 1
CR1L	1.973131	3.61E-08	9.42E-07	5.508937	Up	complement C3b/C4b receptor 1 like
CATSPERB	1.971487	1.57E-09	6.63E-08	6.036545	Up	cation channel sperm-associated auxiliary subunit beta
ANAPC1P5	1.967991	1.57E-05	0.000153	4.318341	Up	ANAPC1 pseudogene 5
GLUL	1.964718	5.25E-52	6.29E-48	15.17406	Up	glutamate-ammonia ligase
BCAT1	1.96429	1.08E-17	4.04E-15	8.565251	Up	branched chain amino acid transaminase 1
NAMPTP1	1.956402	4.51E-08	1.14E-06	5.469617	Up	nicotinamidephosphoribosyltransferasepseudogene 1
CXCL11	1.956011	0.002264	0.009041	3.053218	Up	C-X-C motif chemokine ligand 11
RPL23AP57	1.954543	2.93E-06	3.83E-05	4.675892	Up	ribosomal protein L23a pseudogene 57
CLEC1B	1.954137	0.002089	0.008454	3.077239	Up	C-type lectin domain family 1 member B

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
SNORD89	1.952967	2.63E-11	2.02E-09	6.665678	Up	small nucleolar RNA, C/D box 89
ST6GALNAC3	1.952404	1.55E-24	1.86E-21	10.22387	Up	ST6 N-acetylgalactosaminidase alpha-2,6-sialyl-transferase 3
TIMD4	1.944744	0.002384	0.009444	3.037709	Up	T cell immunoglobulin and mucin domain containing 4
PI15	1.934166	9.42E-05	0.000672	3.904986	Up	peptidase inhibitor 15
ACTG1P12	1.927876	0.004909	0.017027	2.812926	Up	actin gamma 1 pseudogene 12
DHRS7C	1.926808	0.00016	0.001039	3.774868	Up	dehydrogenase/reductase 7C
C4orf54	1.919958	0.000731	0.003612	3.377741	Up	chromosome 4 open reading frame 54
CD53	1.91885	1.82E-14	3.27E-12	7.662853	Up	CD53 molecule
TFCP2L1	1.910287	4.98E-15	1.03E-12	7.827499	Up	transcription factor CP2 like 1
OTOGL	1.906497	1.77E-07	3.63E-06	5.221944	Up	otogelin like
MRC1	1.904979	6.16E-16	1.58E-13	8.086196	Up	mannose receptor C-type 1
CYP4A44P	1.904841	0.00441	0.015621	2.847239	Up	cytochrome P450 family 4 subfamily A member 44, pseudogene
TENT5B	1.903378	3.16E-12	3.14E-10	6.970532	Up	terminal nucleotidyltransferase 5B
SNORA54	1.898421	2.16E-09	8.61E-08	5.985073	Up	small nucleolar RNA, H/ACA box 54
TFRC	1.897404	7.58E-11	5.08E-09	6.508634	Up	transferrin receptor
NAMPT	1.897309	1.50E-09	6.34E-08	6.044689	Up	nicotinamidephosphoribosyltransferase
RPL36AP49	1.896784	0.000113	0.000778	3.861828	Up	ribosomal protein L36a pseudogene 49
CPM	1.896726	1.71E-14	3.10E-12	7.671005	Up	carboxypeptidase M
BIRC3	1.895028	3.24E-09	1.21E-07	5.918851	Up	baculoviral IAP repeat containing 3
FPR2	1.892003	9.18E-12	8.15E-10	6.818737	Up	formyl peptide receptor 2
DCXR-DT	1.891386	6.09E-05	0.000467	4.009235	Up	DCXR divergent transcript
SAA1	1.884901	0.008132	0.02567	2.646559	Up	serum amyloid A1
RNVU1-17	1.881652	0.011803	0.03465	2.517978	Up	RNA, variant U1 small nuclear 17
RRM2	1.881454	1.29E-05	0.00013	4.361373	Up	ribonucleotide reductase regulatory subunit M2
IGHV3-75	1.875375	0.0033	0.012291	2.938352	Up	immunoglobulin heavy variable 3-75 (pseudogene)
ADH1C	1.873873	2.37E-09	9.28E-08	5.970312	Up	alcohol dehydrogenase 1C (class I), gamma polypeptide
CCL26	1.869224	0.007182	0.023197	2.68828	Up	C-C motif chemokine ligand 26
FCN3	1.867346	1.65E-07	3.42E-06	5.23522	Up	ficolin 3
SNORA24B	1.866393	0.002805	0.010762	2.988369	Up	small nucleolar RNA, H/ACA box 24B
H2BC10	1.863206	2.66E-06	3.52E-05	4.695647	Up	H2B clustered histone 10
RNU5B-1	1.862574	2.40E-08	6.69E-07	5.580627	Up	RNA, U5B small nuclear 1
NREP-AS1	1.855772	0.003909	0.014152	2.885407	Up	NREP antisense RNA 1
SLC30A10	1.852745	3.17E-09	1.19E-07	5.922534	Up	solute carrier family 30 member 10
KMO	1.846148	8.75E-08	2.02E-06	5.350894	Up	kynurenine 3-monooxygenase
AGTR1	1.842207	1.57E-08	4.65E-07	5.653996	Up	angiotensin II receptor type 1
STRIT1	1.834893	0.002172	0.008721	3.065687	Up	small transmembrane regulator of ion transport 1
LRRN3	1.832508	6.47E-10	3.15E-08	6.178558	Up	leucine rich repeat neuronal 3
GLULP4	1.827979	1.40E-19	8.12E-17	9.05222	Up	glutamate-ammonia ligase pseudogene 4
SCARNA1	1.824848	5.88E-06	6.82E-05	4.530558	Up	small Cajal body-specific RNA 1
H2BC14	1.82124	0.003105	0.011669	2.957161	Up	H2B clustered histone 14
HRAT17	1.818053	4.55E-08	1.15E-06	5.467918	Up	heart tissue-associated transcript 17
RPS17P5	1.816377	0.001238	0.005545	3.229989	Up	ribosomal protein S17 pseudogene 5
TMEM100	1.810968	8.49E-08	1.97E-06	5.356358	Up	transmembrane protein 100
CHST9	1.807261	7.42E-07	1.20E-05	4.949947	Up	carbohydrate sulfotransferase 9
C5orf64	1.804206	0.000424	0.002303	3.524769	Up	chromosome 5 putative open reading frame 64
GPR84	1.80394	0.001523	0.006551	3.170358	Up	G protein-coupled receptor 84

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
P2RY12	1.803474	1.78E-10	1.05E-08	6.379533	Up	purinergic receptor P2Y12
AQP3	1.80279	8.38E-17	2.50E-14	8.325739	Up	aquaporin 3 (Gill blood group)
FLT3	1.802445	1.14E-06	1.73E-05	4.864933	Up	fms related receptor tyrosine kinase 3
TUBAL3	1.800851	1.63E-06	2.35E-05	4.794022	Up	tubulin alpha like 3
RNU6-432P	1.800813	0.012579	0.036413	2.495479	Up	RNA, U6 small nuclear 432, pseudogene
ADGRF4	1.80056	0.009021	0.027887	2.611244	Up	adhesion G protein-coupled receptor F4
RPSAP72	1.794723	0.000181	0.001149	3.744428	Up	ribosomal protein SA pseudogene 72
TDRD9	1.793742	6.22E-10	3.05E-08	6.184868	Up	tudor domain containing 9
H2BC9	1.793678	1.74E-05	0.000167	4.295499	Up	H2B clustered histone 9
TFEC	1.792475	2.41E-10	1.35E-08	6.332482	Up	transcription factor EC
HPR	1.789521	1.17E-15	2.77E-13	8.007726	Up	haptoglobin-related protein
OR52N1	1.783269	7.79E-05	0.000573	3.950822	Up	olfactory receptor family 52 subfamily N member 1
SIGLEC5	1.77985	0.012403	0.036055	2.500456	Up	sialic acid binding Ig like lectin 5
HSD11B1	1.777559	2.71E-07	5.20E-06	5.14268	Up	hydroxysteroid 11-beta dehydrogenase 1
SIGLEC7	1.775476	3.41E-08	8.96E-07	5.519139	Up	sialic acid binding Ig like lectin 7
RAB39A	1.77509	2.68E-08	7.38E-07	5.560859	Up	RAB39A, member RAS oncogene family
MSR1	1.763236	7.41E-11	4.98E-09	6.512189	Up	macrophage scavenger receptor 1
TTK	1.759317	1.34E-06	1.98E-05	4.833428	Up	TTK protein kinase
SRGN	1.758712	1.49E-09	6.33E-08	6.045505	Up	serglycin
IGKV1-9	1.752989	0.008732	0.027147	2.622361	Up	immunoglobulin kappa variable 1-9
MANCR	1.749224	2.08E-06	2.87E-05	4.745385	Up	mitotically associated long non-coding RNA
H2BC3	1.747613	4.57E-07	8.01E-06	5.043531	Up	H2B clustered histone 3
GPR151	1.747447	0.002455	0.009668	3.028868	Up	G protein-coupled receptor 151
EEF1AKMT4	1.745965	8.00E-11	5.27E-09	6.500552	Up	EEF1A lysine methyltransferase 4
RNU6-8	1.74219	0.000499	0.002629	3.481465	Up	RNA, U6 small nuclear 8
RNU6-7	1.739324	0.005441	0.018477	2.779719	Up	RNA, U6 small nuclear 7
GPR34	1.739002	2.53E-06	3.39E-05	4.705393	Up	G protein-coupled receptor 34
PRRG4	1.736915	1.60E-08	4.72E-07	5.650901	Up	proline rich and Gla domain 4
ZNF622P1	1.734007	1.34E-11	1.11E-09	6.764356	Up	ZNF622 pseudogene 1
SAMSN1	1.730904	1.22E-10	7.60E-09	6.437276	Up	SAM domain, SH3 domain and nuclear localization signals 1
RPL7P16	1.72837	0.004511	0.015924	2.840023	Up	ribosomal protein L7 pseudogene 16
TMPRSS12	1.727275	0.000581	0.002988	3.440491	Up	transmembrane serine protease 12
TREML4	1.727104	0.00408	0.014674	2.871883	Up	triggering receptor expressed on myeloid cells like 4
S100A3	1.72334	0.000194	0.001221	3.726257	Up	S100 calcium binding protein A3
CADM2	1.723248	2.00E-05	0.000186	4.26507	Up	cell adhesion molecule 2
SNORD96B	1.722442	0.000122	0.00083	3.842047	Up	small nucleolar RNA, C/D box 96B
SLAMF8	1.721893	1.59E-05	0.000154	4.316518	Up	SLAM family member 8
MCTP2	1.709952	2.95E-05	0.000258	4.177374	Up	multiple C2 and transmembrane domain containing 2
AQP4	1.708509	0.000906	0.004302	3.318096	Up	aquaporin 4
RPSAP47	1.706609	1.73E-10	1.02E-08	6.383673	Up	ribosomal protein SA pseudogene 47
FCER1G	1.705951	2.92E-14	4.85E-12	7.602027	Up	Fc fragment of IgE receptor Ig
SIGLEC9	1.698602	3.97E-08	1.02E-06	5.492354	Up	sialic acid binding Ig like lectin 9
HS6ST2	1.695316	1.33E-05	0.000134	4.354606	Up	heparansulfate 6-O-sulfotransferase 2
NQO1	1.694258	9.79E-10	4.45E-08	6.112814	Up	NAD(P)H quinone dehydrogenase 1
MELK	1.69103	0.000175	0.00112	3.752058	Up	maternal embryonic leucine zipper kinase
CR1	1.687769	1.07E-09	4.76E-08	6.099248	Up	complement C3b/C4b receptor 1 (Knops blood group)

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
LGR5	1.685453	0.006707	0.021942	2.711033	Up	leucine rich repeat containing G protein-coupled receptor 5
TREM2	1.685313	1.80E-07	3.68E-06	5.218981	Up	triggering receptor expressed on myeloid cells 2
C5orf47	1.682576	0.000533	0.00278	3.463457	Up	chromosome 5 open reading frame 47
TDGF1P3	1.682479	0.015866	0.043917	2.411988	Up	teratocarcinoma-derived growth factor 1 pseudogene 3
RPL17P5	1.675486	0.001939	0.007957	3.099414	Up	ribosomal protein L17 pseudogene 5
AASS	1.670227	1.39E-14	2.57E-12	7.696848	Up	aminoadipate-semialdehyde synthase
CCL18	1.66744	0.003106	0.01167	2.957086	Up	C-C motif chemokine ligand 18
TRHDE	1.66553	0.001624	0.006901	3.151601	Up	thyrotropin releasing hormone degrading enzyme
HP	1.66454	2.82E-16	7.79E-14	8.18082	Up	haptoglobin
MFN1P1	1.663417	0.000624	0.003179	3.420892	Up	MFN1 pseudogene 1
TAS2R8	1.663194	9.49E-05	0.000676	3.903386	Up	taste 2 receptor member 8
SNORA35B	1.662779	0.001178	0.005334	3.244172	Up	small nucleolar RNA, H/ACA box 35B
SNORA23	1.661962	1.77E-05	0.000169	4.292401	Up	small nucleolar RNA, H/ACA box 23
RNU6-1201P	1.661054	0.00885	0.027432	2.617797	Up	RNA, U6 small nuclear 1201, pseudogene
TC2N	1.658839	8.02E-08	1.87E-06	5.366685	Up	tandem C2 domains, nuclear
IRAK3	1.654092	9.42E-13	1.08E-10	7.138756	Up	interleukin 1 receptor-associated kinase 3
MANEA	1.64711	1.84E-07	3.75E-06	5.214785	Up	mannosidaseendo-alpha
LY96	1.645511	1.14E-08	3.52E-07	5.709057	Up	lymphocyte antigen 96
MS4A6A	1.642181	2.23E-11	1.76E-09	6.689876	Up	membrane spanning 4-domains A6A
EEF1B2P2	1.637475	5.55E-16	1.44E-13	8.098744	Up	eukaryotic translation elongation factor 1 beta 2 pseudogene 2
OR52N3P	1.636963	0.008797	0.027323	2.619835	Up	olfactory receptor family 52 subfamily N member 3 pseudogene
CCDC68	1.635162	3.04E-08	8.14E-07	5.539097	Up	coiled-coil domain containing 68
OXGR1	1.631569	0.001906	0.007845	3.104526	Up	oxoglutarate receptor 1
SNORA14A	1.629388	5.58E-06	6.53E-05	4.541763	Up	small nucleolar RNA, H/ACA box 14A
SNORA63D	1.628392	5.51E-10	2.75E-08	6.203763	Up	small nucleolar RNA, H/ACA box 63D
BATF	1.626564	0.001109	0.005076	3.261262	Up	basic leucine zipper ATF-like transcription factor
SNORA12	1.620842	1.45E-05	0.000143	4.335552	Up	small nucleolar RNA, H/ACA box 12
CYBB	1.620824	4.99E-09	1.73E-07	5.847624	Up	cytochrome b-245 beta chain
SNORA20	1.617678	4.39E-06	5.33E-05	4.592027	Up	small nucleolar RNA, H/ACA box 20
RPL39	1.616617	2.14E-07	4.26E-06	5.186666	Up	ribosomal protein L39
ENO1-AS1	1.614146	0.012136	0.035447	2.508163	Up	ENO1 antisense RNA 1
KCNH7	1.613275	0.000284	0.001664	3.629283	Up	potassium voltage-gated channel subfamily H member 7
WDR49	1.613104	1.07E-06	1.64E-05	4.878054	Up	WD repeat domain 49
CDK1	1.607981	6.99E-07	1.14E-05	4.961638	Up	cyclin-dependent kinase 1
SGPP2	1.606731	1.22E-05	0.000125	4.374084	Up	sphingosine-1-phosphate phosphatase 2
RNA5-8SN2	1.60281	0.018041	0.048624	2.364776	Up	RNA, 5.8S ribosomal N2
RNA5-8SP10	1.601955	0.01812	0.048804	2.36316	Up	RNA, 5.8S ribosomal pseudogene 10
ELL2	1.60165	8.49E-10	3.95E-08	6.135495	Up	elongation factor for RNA polymerase II 2
RNA5-8SN3	1.600955	0.018211	0.049008	2.361309	Up	RNA, 5.8S ribosomal N3
RNA5-8SN1	1.600276	0.018263	0.049117	2.360237	Up	RNA, 5.8S ribosomal N1
RPL23AP43	1.59674	4.38E-09	1.54E-07	5.869243	Up	ribosomal protein L23a pseudogene 43
RPL11P2	1.589405	0.001046	0.004841	3.277911	Up	ribosomal protein L11 pseudogene 2
RIDA	1.58823	1.72E-07	3.55E-06	5.227317	Up	reactive intermediate imine deaminase A homolog
RNU6-733P	1.585162	0.003849	0.013981	2.890312	Up	RNA, U6 small nuclear 733, pseudogene

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
RPL17P34	1.58308	0.000144	0.000952	3.800932	Up	ribosomal protein L17 pseudogene 34
SLC7A11	1.581975	0.001229	0.005513	3.232107	Up	solute carrier family 7 member 11
SIRPB2	1.581299	8.44E-13	9.94E-11	7.15385	Up	signal regulatory protein beta 2
DRC1	1.58022	0.01391	0.039445	2.459583	Up	dynein regulatory complex subunit 1
NDUFA4	1.577302	0.000125	0.000848	3.835636	Up	NDUFA4 mitochondrial complex associated
NECAB1	1.575598	1.27E-06	1.88E-05	4.844721	Up	N-terminal EF-hand calcium binding protein 1
TMTC1	1.572658	1.06E-30	3.47E-27	11.5186	Up	transmembrane O-mannosyltransferase targeting cadherins 1
PAFAH1B2P2	1.57226	0.001585	0.006768	3.158708	Up	PAFAH1B2 pseudogene 2
RN7SKP83	1.572085	0.007758	0.024699	2.662424	Up	RN7SK pseudogene 83
SNORD15B	1.571392	8.70E-06	9.42E-05	4.447155	Up	small nucleolar RNA, C/D box 15B
LRMDA	1.569279	1.14E-12	1.27E-10	7.112018	Up	leucine rich melanocyte differentiation associated
H2AC14	1.568373	7.29E-05	0.000542	3.96672	Up	H2A clustered histone 14
SYN2	1.568293	0.000429	0.002324	3.521584	Up	synapsin II
H3C12	1.568271	0.001592	0.006787	3.157385	Up	H3 clustered histone 12
GNMT	1.566584	1.03E-07	2.31E-06	5.321975	Up	glycine N-methyltransferase
C1orf162	1.566215	7.55E-19	3.62E-16	8.86654	Up	chromosome 1 open reading frame 162
STARD7	1.56547	5.23E-12	4.91E-10	6.899143	Up	StAR related lipid transfer domain containing 7
CTH	1.562456	1.73E-10	1.02E-08	6.383435	Up	cystathionine gamma-lyase
RPSAP53	1.561259	3.06E-10	1.66E-08	6.295672	Up	ribosomal protein SA pseudogene 53
TOP2A	1.560869	3.88E-05	0.000325	4.114363	Up	DNA topoisomerase II alpha
H3C8	1.560579	0.000125	0.000848	3.835581	Up	H3 clustered histone 8
DSPP	1.557954	0.000659	0.003323	3.406199	Up	dentin sialophosphoprotein
C1orf105	1.553019	2.24E-05	0.000205	4.239316	Up	chromosome 1 open reading frame 105
PLA1A	1.552684	1.50E-10	9.02E-09	6.40555	Up	phospholipase A1 member A
MYO16-AS1	1.550275	0.014208	0.040139	2.451962	Up	MYO16 antisense RNA 1
CARD18	1.550039	0.006733	0.021997	2.709773	Up	caspase recruitment domain family member 18
SCARNA8	1.549956	0.005527	0.018713	2.774618	Up	small Cajal body-specific RNA 8
RPSAP8	1.548701	1.84E-07	3.75E-06	5.214839	Up	ribosomal protein SA pseudogene 8
RHOU	1.547008	3.03E-16	8.31E-14	8.172136	Up	ras homolog family member U
CFTR	1.544694	1.88E-05	0.000177	4.279055	Up	CF transmembrane conductance regulator
H2BC11	1.542889	1.15E-15	2.76E-13	8.009334	Up	H2B clustered histone 11
H1-5	1.5423	7.80E-05	0.000574	3.95033	Up	H1.5 linker histone, cluster member
H4C6	1.542163	3.05E-06	3.97E-05	4.66725	Up	H4 clustered histone 6
CNTN3	1.541098	1.20E-05	0.000123	4.378264	Up	contactin 3
TAS2R9	1.538989	0.000415	0.002267	3.53023	Up	taste 2 receptor member 9
CLEC7A	1.538473	1.04E-07	2.33E-06	5.319967	Up	C-type lectin domain containing 7A
UAP1	1.537928	9.32E-14	1.38E-11	7.450184	Up	UDP-N-acetylglucosamine pyrophosphorylase 1
F8	1.536294	9.66E-10	4.40E-08	6.114986	Up	coagulation factor VIII
RPL22L1	1.536016	1.20E-15	2.81E-13	8.004165	Up	ribosomal protein L22 like 1
FKBP5	1.535956	3.39E-05	0.000291	4.145574	Up	FKBP prolyl isomerase 5
CTSC	1.53189	6.31E-10	3.09E-08	6.182497	Up	cathepsin C
CATIP	1.531775	0.003739	0.013631	2.8994	Up	ciliogenesis-associated TTC17 interacting protein
MROH2B	1.529396	3.37E-06	4.30E-05	4.64712	Up	maestro heat like repeat family member 2B
AMD1	1.529031	4.53E-09	1.58E-07	5.863403	Up	adenosylmethionine decarboxylase 1
JCHAIN	1.528867	0.002329	0.009254	3.044656	Up	joining chain of multimeric IgA and IgM
RPS29	1.528524	2.36E-09	9.27E-08	5.971114	Up	ribosomal protein S29
SLC17A3	1.526651	0.000251	0.001501	3.661437	Up	solute carrier family 17 member 3
RPL34P9	1.526313	0.007877	0.025035	2.65731	Up	ribosomal protein L34 pseudogene 9
CCAT2	1.522385	0.013092	0.037581	2.48125	Up	colon cancer-associated transcript 2

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
C3AR1	1.521761	1.27E-07	2.73E-06	5.283316	Up	complement C3a receptor 1
ATP5MD	1.521226	3.58E-05	0.000304	4.132721	Up	ATP synthase membrane subunit DAPIT
TOMM20L	1.518109	0.007005	0.022721	2.696599	Up	translocase of outer mitochondrial membrane 20 like
TDGF1	1.517903	0.009707	0.029561	2.586099	Up	teratocarcinoma-derived growth factor 1
SMIM9	1.517204	2.10E-07	4.19E-06	5.189957	Up	small integral membrane protein 9
RPS17P16	1.515806	1.10E-08	3.42E-07	5.715068	Up	ribosomal protein S17 pseudogene 16
SNORD114-1	1.51367	0.010154	0.030658	2.57053	Up	small nucleolar RNA, C/D box 114-1
SPARCL1	1.511936	1.13E-12	1.27E-10	7.11313	Up	SPARC like 1
IGHV3-48	1.509589	0.017192	0.046753	2.382576	Up	immunoglobulin heavy variable 3-48
IGSF11-AS1	1.509326	0.000633	0.003217	3.416935	Up	IGSF11 antisense RNA 1
MTHFD2	1.507945	8.50E-13	9.96E-11	7.152895	Up	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase
RNU7-47P	1.507736	0.016611	0.045533	2.395199	Up	RNA, U7 small nuclear 47 pseudogene
MRPS36	1.500806	1.11E-07	2.46E-06	5.307513	Up	mitochondrial ribosomal protein S36
RPS15AP19	1.500194	1.44E-05	0.000142	4.337962	Up	ribosomal protein S15a pseudogene 19
ASS1P13	1.500114	0.004139	0.014847	2.867358	Up	argininosuccinate synthetase 1 pseudogene 13
RPS15AP12	1.499685	5.04E-07	8.68E-06	5.02479	Up	ribosomal protein S15a pseudogene 12
CCN6	1.498809	5.40E-07	9.21E-06	5.01144	Up	cellular communication network factor 6
RNVU1-15	1.497703	0.00577	0.019377	2.760558	Up	RNA, variant U1 small nuclear 15
ANKRD2	1.492058	0.001325	0.005862	3.210581	Up	ankyrin repeat domain 2
CERS6-AS1	1.490253	0.00075	0.003686	3.370516	Up	CERS6 antisense RNA 1
MYO16	1.484418	2.11E-11	1.68E-09	6.698139	Up	myosin XVI
RNU5D-1	1.480081	0.000625	0.00318	3.420598	Up	RNA, U5D small nuclear 1
RNU6-883P	1.479939	0.000339	0.001924	3.583552	Up	RNA, U6 small nuclear 883, pseudogene
XK	1.476882	2.36E-09	9.28E-08	5.970688	Up	X-linked Kx blood group
CHL1	1.470314	0.000109	0.000756	3.87004	Up	cell adhesion molecule L1 like
SERPINI2	1.467813	0.000862	0.004124	3.33222	Up	serpin family I member 2
RPL10AP2	1.46755	6.84E-10	3.30E-08	6.169763	Up	ribosomal protein L10a pseudogene 2
CDCP1	1.467118	2.77E-06	3.66E-05	4.687194	Up	CUB domain containing protein 1
RPL24P7	1.46645	0.005976	0.019931	2.749073	Up	RPL24 pseudogene 7
HIGD1A	1.466146	1.66E-05	0.00016	4.306171	Up	HIG1 hypoxia inducible domain family member 1A
RPL21P134	1.464332	2.14E-06	2.95E-05	4.739288	Up	ribosomal protein L21 pseudogene 134
RPL26P36	1.461518	4.79E-05	0.000384	4.065713	Up	ribosomal protein L26 pseudogene 36
CD38	1.46149	1.53E-12	1.63E-10	7.072127	Up	CD38 molecule
RNASE6	1.460364	8.21E-08	1.91E-06	5.362446	Up	ribonuclease A family member k6
RPS6P26	1.460064	0.013738	0.039042	2.464042	Up	ribosomal protein S6 pseudogene 26
RAD9B	1.458667	2.57E-06	3.42E-05	4.702851	Up	RAD9 checkpoint clamp component B
CD180	1.457665	2.04E-07	4.08E-06	5.196045	Up	CD180 molecule
MAOA	1.455187	4.24E-11	3.02E-09	6.595554	Up	monoamine oxidase A
STC1	1.453056	4.49E-07	7.88E-06	5.047112	Up	stanniocalcin 1
RPL26	1.452966	1.55E-08	4.60E-07	5.655783	Up	ribosomal protein L26
RNU6-861P	1.45206	0.00044	0.002372	3.514638	Up	RNA, U6 small nuclear 861, pseudogene
RNU4ATAC	1.450727	1.21E-07	2.64E-06	5.291672	Up	RNA, U4atac small nuclear (U12-dependent splicing)
RPS15A	1.450304	1.54E-08	4.58E-07	5.656644	Up	ribosomal protein S15a
COX7A2	1.449687	4.24E-05	0.000349	4.093758	Up	cytochrome c oxidase subunit 7A2
COX7B	1.449099	8.98E-05	0.000647	3.916554	Up	cytochrome c oxidase subunit 7B
ASS1P3	1.44836	0.001209	0.005443	3.236753	Up	argininosuccinate synthetase 1 pseudogene 3

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
BMPRI1B	1.447825	0.000263	0.001561	3.649046	Up	bone morphogenetic protein receptor type 1B
SNORA74D	1.446225	2.53E-07	4.89E-06	5.155778	Up	small nucleolar RNA, H/ACA box 74D
SNORD46	1.446097	1.64E-05	0.000159	4.30866	Up	small nucleolar RNA, C/D box 46
RNU6-85P	1.445226	0.010186	0.030721	2.569448	Up	RNA, U6 small nuclear 85, pseudogene
KLHL40	1.445085	0.000238	0.001438	3.675217	Up	kelch-like family member 40
PSMB3P1	1.44425	0.003972	0.01434	2.880396	Up	proteasome subunit beta 3 pseudogene 1
RNU5E-1	1.442091	6.35E-05	0.000483	3.999534	Up	RNA, U5E small nuclear 1
OSTC	1.441725	1.03E-06	1.59E-05	4.885034	Up	oligosaccharyltransferase complex non-catalytic subunit
IGHV3-53	1.440864	0.004522	0.015953	2.839243	Up	immunoglobulin heavy variable 3-53
H2AC12	1.439996	1.95E-07	3.93E-06	5.204473	Up	H2A clustered histone 12
TMEM126A	1.439784	2.71E-05	0.000241	4.196445	Up	transmembrane protein 126A
RPL21P98	1.439262	3.21E-07	5.99E-06	5.110412	Up	ribosomal protein L21 pseudogene 98
RPSAP18	1.43871	7.85E-15	1.59E-12	7.769966	Up	ribosomal protein SA pseudogene 18
SLPI	1.437392	0.001741	0.007297	3.131244	Up	secretory leukocyte peptidase inhibitor
SNX10	1.435195	1.56E-06	2.26E-05	4.803244	Up	sorting nexin 10
SERPINF2	1.434614	6.30E-05	0.000479	4.001415	Up	serpin family F member 2
APOB	1.433745	4.01E-06	4.95E-05	4.610912	Up	apolipoprotein B
PHACTR3-AS1	1.432722	0.003127	0.011742	2.954996	Up	PHACTR3 antisense RNA 1
KCNK2	1.431741	0.001982	0.008096	3.092883	Up	potassium two pore domain channel subfamily K member 2
FGF7	1.430857	3.69E-05	0.000312	4.126136	Up	fibroblast growth factor 7
RPL21P37	1.425707	7.28E-06	8.16E-05	4.485267	Up	ribosomal protein L21 pseudogene 37
RGCC	1.423871	4.13E-09	1.48E-07	5.878712	Up	regulator of cell cycle
SCGB1D2	1.423588	0.006582	0.021579	2.717307	Up	secretoglobin family 1D member 2
GRB14	1.422874	1.60E-06	2.30E-05	4.79862	Up	growth factor receptor bound protein 14
CALCRL	1.422375	0.000325	0.001859	3.594553	Up	calcitonin receptor like receptor
ZNF57	1.421947	9.28E-16	2.25E-13	8.036067	Up	zinc finger protein 57
ZWINT	1.421537	0.001447	0.006299	3.185112	Up	ZW10 interacting kinetochore protein
PRDX1	1.421094	1.48E-09	6.28E-08	6.046997	Up	peroxiredoxin 1
SPINK6	1.42106	0.000208	0.001292	3.709213	Up	serine peptidase inhibitor Kazal type 6
SDR16C5	1.420747	0.001632	0.006924	3.150211	Up	short chain dehydrogenase/reductase family 16C member 5
SAT1	1.419759	3.07E-13	3.99E-11	7.291188	Up	spermidine/spermine N1-acetyltransferase 1
CMTM5	1.416424	0.010686	0.031955	2.552795	Up	CKLF like MARVEL transmembrane domain containing 5
GPR12	1.416355	0.001055	0.004875	3.275431	Up	G protein-coupled receptor 12
ANGPTL1	1.41578	5.67E-06	6.62E-05	4.538219	Up	angiotensin-like 1
TMEM258	1.414885	1.79E-09	7.34E-08	6.015608	Up	transmembrane protein 258
OVCH1	1.41236	1.27E-07	2.73E-06	5.283233	Up	ovochymase 1
LCP1	1.411907	3.95E-09	1.42E-07	5.886312	Up	lymphocyte cytosolic protein 1
HPSE	1.411385	1.45E-09	6.21E-08	6.049631	Up	heparanase
MS4A6E	1.410285	3.05E-05	0.000266	4.17003	Up	membrane spanning 4-domains A6E
LAPTM5	1.409598	3.39E-14	5.49E-12	7.582467	Up	lysosomal protein transmembrane 5
RPS13	1.408548	2.28E-05	0.000208	4.235151	Up	ribosomal protein S13
MARK3	1.408321	1.74E-27	3.29E-24	10.86237	Up	microtubule affinity regulating kinase 3
RNU6-314P	1.408007	0.008827	0.027382	2.618689	Up	RNA, U6 small nuclear 314, pseudogene
PABPC5-AS1	1.407981	0.0026	0.010122	3.011424	Up	PABPC5 antisense RNA 1
KIF20A	1.406715	1.60E-05	0.000155	4.313939	Up	kinesin family member 20A
TMEM97	1.405702	2.93E-08	7.89E-07	5.545813	Up	transmembrane protein 97

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
GALNT15	1.40252	0.000217	0.001335	3.698475	Up	polypeptide N-acetylgalactosaminyltransferase 15
TNFRSF11A	1.402472	1.04E-11	8.98E-10	6.801005	Up	TNF receptor superfamily member 11a
EEF1E1	1.40119	1.37E-08	4.12E-07	5.677664	Up	eukaryotic translation elongation factor 1 epsilon 1
RPS27	1.399161	2.58E-06	3.44E-05	4.701756	Up	ribosomal protein S27
SNRPG	1.39839	1.13E-05	0.000116	4.391256	Up	small nuclear ribonucleoprotein polypeptide G
TKTL1	1.398184	1.09E-06	1.66E-05	4.874043	Up	transketolase like 1
RPL36AP46	1.396676	8.98E-08	2.05E-06	5.346292	Up	ribosomal protein L36a pseudogene 46
UGT2B4	1.396506	0.000883	0.004211	3.325499	Up	UDP glucuronosyltransferase family 2 member B4
IL18RAP	1.395923	2.98E-05	0.000261	4.175301	Up	interleukin 18 receptor accessory protein
RPS7P1	1.394955	4.19E-07	7.43E-06	5.060171	Up	ribosomal protein S7 pseudogene 1
MRPL50	1.393049	1.37E-05	0.000136	4.349111	Up	mitochondrial ribosomal protein L50
CLEC12A	1.390248	0.001819	0.007561	3.118329	Up	C-type lectin domain family 12 member A
PDE7A	1.389661	1.23E-08	3.79E-07	5.694899	Up	phosphodiesterase 7A
TIMP3	1.389553	1.80E-18	8.28E-16	8.769373	Up	TIMP metalloproteinase inhibitor 3
TMSB4XP4	1.389091	2.81E-06	3.71E-05	4.683997	Up	TMSB4X pseudogene 4
EMB	1.384816	3.95E-06	4.90E-05	4.613757	Up	embigin
AP1S2	1.381599	9.29E-05	0.000664	3.908452	Up	adaptor related protein complex 1 subunit sigma 2
PDE4D	1.381594	3.77E-09	1.37E-07	5.894038	Up	phosphodiesterase 4D
CYP4X1	1.376257	1.39E-12	1.50E-10	7.084667	Up	cytochrome P450 family 4 subfamily X member 1
C7	1.37554	6.25E-08	1.51E-06	5.411628	Up	complement C7
SHC4	1.372456	1.67E-07	3.46E-06	5.232558	Up	SHC adaptor protein 4
RNY3	1.371967	0.000713	0.003539	3.384396	Up	RNA, Ro60-associated Y3
DEPDC1B	1.371127	0.006113	0.020317	2.741635	Up	DEP domain containing 1B
GLIS1	-4.88911	8.26E-09	2.66E-07	-5.76313	Down	GLIS family zinc finger 1
TMEM130	-4.13365	1.60E-05	0.000155	-4.31446	Down	transmembrane protein 130
PRND	-4.11724	0.00016	0.001038	-3.77541	Down	prion like protein doppel
RTN4RL2	-4.02078	1.13E-07	2.49E-06	-5.30509	Down	reticulon 4 receptor like 2
CRACD	-3.86097	1.35E-09	5.85E-08	-6.06087	Down	capping protein inhibiting regulator of actin dynamics
GRIFIN	-3.84956	9.97E-07	1.54E-05	-4.89228	Down	galectin-related inter-fiber protein
GPR78	-3.68804	1.76E-05	0.000168	-4.29352	Down	G protein-coupled receptor 78
LRRCS5	-3.68204	6.31E-18	2.58E-15	-8.6267	Down	leucine rich repeat containing 55
CYP2A13	-3.58005	1.82E-05	0.000172	-4.28569	Down	cytochrome P450 family 2 subfamily A member 13
ESM1	-3.56771	4.07E-08	1.04E-06	-5.48761	Down	endothelial cell specific molecule 1
CAPN6	-3.54782	8.41E-07	1.34E-05	-4.92561	Down	calpain 6
EEF1DP5	-3.50705	0.011542	0.034017	-2.52584	Down	eukaryotic translation elongation factor 1 delta pseudogene 5
ELFN2	-3.48594	1.02E-05	0.000107	-4.41371	Down	extracellular leucine rich repeat and fibronectin type III domain containing 2
AGKP1	-3.41899	1.32E-06	1.95E-05	-4.83704	Down	AGK pseudogene 1
SMIM41	-3.40035	0.003837	0.01395	-2.89127	Down	small integral membrane protein 41
ACE	-3.39135	4.80E-60	1.73E-55	-16.344	Down	angiotensin I converting enzyme
FBN3	-3.3666	4.31E-06	5.25E-05	-4.59606	Down	fibrillin 3
MTCYBP2	-3.36649	6.17E-06	7.10E-05	-4.52059	Down	MT-CYB pseudogene 2
CELA2A	-3.34078	0.000882	0.004211	-3.32556	Down	chymotrypsin like elastase 2A
ASPDH	-3.33645	7.67E-07	1.24E-05	-4.9437	Down	aspartate dehydrogenase domain containing
LY6H	-3.3042	0.002921	0.011115	-2.9759	Down	lymphocyte antigen 6 family member H
PENK	-3.29143	3.03E-09	1.15E-07	-5.92992	Down	proenkephalin

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
FNDC1	-3.2771	8.48E-49	7.62E-45	-14.6814	Down	fibronectin type III domain containing 1
CLEC12A-AS1	-3.27513	0.000824	0.003969	-3.34466	Down	CLEC12A antisense RNA 1
RNU6-255P	-3.25696	2.57E-06	3.42E-05	-4.70288	Down	RNA, U6 small nuclear 255, pseudogene
CCDC114	-3.23009	4.51E-05	0.000366	-4.0797	Down	coiled-coil domain containing 114
TNFRSF4	-3.2264	3.37E-12	3.35E-10	-6.96126	Down	TNF receptor superfamily member 4
TCTE1	-3.20598	0.000519	0.002715	-3.47089	Down	t-complex-associated-testis-expressed 1
FHAD1-AS1	-3.20466	5.63E-06	6.58E-05	-4.53989	Down	FHAD1 antisense RNA 1
CTRB2	-3.19766	0.000172	0.001104	-3.75629	Down	chymotrypsinogen B2
PDE6B-AS1	-3.19396	0.016971	0.046291	-2.38734	Down	PDE6B antisense RNA 1
SYT12	-3.18088	1.76E-06	2.51E-05	-4.77891	Down	synaptotagmin 12
DBH-AS1	-3.17539	8.73E-07	1.38E-05	-4.91835	Down	DBH antisense RNA 1
FATE1	-3.15854	2.19E-06	2.99E-05	-4.73544	Down	fetal and adult testis expressed 1
KNDC1	-3.1471	1.49E-05	0.000146	-4.33039	Down	kinase non-catalytic C-lobe domain containing 1
CASKP1	-3.14455	6.86E-06	7.77E-05	-4.49813	Down	calcium/calmodulin-dependent serine protein kinase pseudogene 1
SLC7A4	-3.14253	6.39E-05	0.000486	-3.99774	Down	solute carrier family 7 member 4
MUC12	-3.13836	0.000144	0.000949	-3.80204	Down	mucin 12, cell surface associated
ZNF385D-AS2	-3.137	0.010737	0.032068	-2.55114	Down	ZNF385D antisense RNA 2
OMP	-3.10801	0.00307	0.011566	-2.96065	Down	olfactory marker protein
HSPB6	-3.10522	3.65E-12	3.59E-10	-6.95009	Down	heat shock protein family B (small) member 6
KDM5D	-3.09165	0.000607	0.003105	-3.42863	Down	lysine demethylase 5D
TTY14	-3.08216	0.000905	0.004299	-3.31842	Down	testis-specific transcript, Y-linked 14
SSC5D	-3.06747	1.63E-22	1.43E-19	-9.76226	Down	scavenger receptor cysteine rich family member with 5 domains
NHLRC4	-3.05493	4.01E-09	1.44E-07	-5.88376	Down	NHL repeat containing 4
AMH	-3.05356	8.17E-06	8.97E-05	-4.46078	Down	anti-Mullerian hormone
COL22A1	-3.04613	5.15E-09	1.78E-07	-5.8423	Down	collagen type XXII alpha 1 chain
PTX4	-3.04335	0.001702	0.007165	-3.1379	Down	pentraxin 4
UTY	-3.03674	0.000311	0.001788	-3.60634	Down	ubiquitously transcribed tetratricopeptide repeat containing, Y-linked
LRFN1	-3.03561	8.30E-05	0.000604	-3.93543	Down	leucine rich repeat and fibronectin type III domain containing 1
TRPM5	-3.03501	0.004501	0.015897	-2.84071	Down	transient receptor potential cation channel sub-family M member 5
APLNR	-3.0197	2.20E-29	5.28E-26	-11.2544	Down	apelin receptor
DDX3Y	-3.00674	0.000247	0.001482	-3.66542	Down	DEAD-box helicase 3 Y-linked
CHD5	-3.00243	5.69E-07	9.59E-06	-5.00144	Down	chromodomain helicase DNA binding protein 5
OFD1P7Y	-2.99908	4.35E-05	0.000357	-4.08781	Down	OFD1 pseudogene 7 Y-linked
FOSB	-2.982	1.29E-07	2.76E-06	-5.28016	Down	FosB proto-oncogene, AP-1 transcription factor subunit
UICLM	-2.97822	0.00174	0.007295	-3.13136	Down	up-regulated in colorectal cancer liver metastasis
CYSRT1	-2.97481	7.91E-06	8.74E-05	-4.46762	Down	cysteine rich tail 1
ATP1B2	-2.97341	6.57E-28	1.31E-24	-10.9511	Down	ATPase Na ⁺ /K ⁺ transporting subunit beta 2
SEZ6L2	-2.96892	3.17E-10	1.71E-08	-6.29043	Down	seizure related 6 homolog like 2
LOXHD1	-2.95005	8.51E-26	1.27E-22	-10.5014	Down	lipoxxygenase homology domains 1
DKKL1	-2.94902	0.0003	0.001736	-3.61569	Down	dickkopf like acrosomal protein 1
CTD-3080P12.3	-2.93164	0.000223	0.001364	-3.69133	Down	uncharacterized LOC101928857
TLR9	-2.92385	0.001216	0.005467	-3.23521	Down	toll-like receptor 9
GET4	-2.9126	4.19E-05	0.000346	-4.0969	Down	guided entry of tail-anchored proteins factor 4
BARHL1	-2.91083	0.001658	0.007018	-3.14546	Down	BarH like homeobox 1
KRTAP5-1	-2.90524	2.52E-07	4.88E-06	-5.15598	Down	keratin-associated protein 5-1

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
CCL3L1	-2.90351	2.27E-06	3.09E-05	-4.72751	Down	C-C motif chemokine ligand 3 like 1
MUC3A	-2.90125	2.33E-17	8.13E-15	-8.47602	Down	mucin 3A, cell surface associated
RBMY2YP	-2.89787	0.001804	0.007512	-3.12081	Down	RNA binding motif protein Y-linked family 2 member Y, pseudogene
OFD1P4Y	-2.89243	0.000176	0.001122	-3.75167	Down	OFD1 pseudogene 4 Y-linked
MED14P1	-2.88792	0.000195	0.001226	-3.72506	Down	mediator complex subunit 14 pseudogene 1
ENTPD8	-2.88316	1.95E-05	0.000183	-4.27	Down	ectonucleoside triphosphate diphosphohydrolase 8
TRIL	-2.88005	1.06E-43	7.61E-40	-13.8632	Down	TLR4 interactor with leucine rich repeats
RN7SKP282	-2.87538	4.94E-05	0.000393	-4.05859	Down	RN7SK pseudogene 282
NXNL1	-2.87209	0.002172	0.008723	-3.0656	Down	nucleoredoxin like 1
RSPH6A	-2.86695	0.001099	0.005037	-3.2639	Down	radial spoke head 6 homolog A
LRRC38	-2.86614	0.000415	0.002268	-3.53009	Down	leucine rich repeat containing 38
RBMY2WP	-2.85224	0.001871	0.007734	-3.11003	Down	RNA binding motif protein Y-linked family 2 member W, pseudogene
RBMY2XP	-2.85224	0.001871	0.007734	-3.11003	Down	RNA binding motif protein Y-linked family 2 member X, pseudogene
FLYWCH1P1	-2.85167	0.012781	0.036883	-2.48983	Down	FLYWCH-type zinc finger 1 pseudogene 1
OFD1P10Y	-2.84945	0.004613	0.016205	-2.83289	Down	OFD1 pseudogene 10 Y-linked
MUC5B	-2.83758	9.25E-10	4.27E-08	-6.12188	Down	mucin 5B, oligomeric mucus/gel-forming
TTY10	-2.83734	0.005326	0.018179	-2.78665	Down	testis-specific transcript, Y-linked 10
GRID2IP	-2.81491	4.63E-07	8.08E-06	-5.04119	Down	Grid2 interacting protein
RNF208	-2.80701	1.03E-09	4.64E-08	-6.10392	Down	ring finger protein 208
SFRP4	-2.80559	9.58E-10	4.38E-08	-6.11626	Down	secreted frizzled related protein 4
ACER1	-2.80336	0.00105	0.004857	-3.27675	Down	alkaline ceramidase 1
EGR1	-2.79643	1.14E-09	5.03E-08	-6.08886	Down	early growth response 1
MAST1	-2.78643	0.000106	0.000738	-3.87721	Down	microtubule-associated serine/threonine kinase 1
ESPN	-2.77946	7.62E-06	8.47E-05	-4.47559	Down	espin
CCDC63	-2.7779	1.74E-07	3.58E-06	-5.22545	Down	coiled-coil domain containing 63
ADAMTS14	-2.77508	5.98E-13	7.35E-11	-7.20105	Down	ADAM metalloproteinase with thrombospondin type 1 motif 14
PRRT1	-2.76987	3.11E-08	8.27E-07	-5.53503	Down	proline rich transmembrane protein 1
COL1A1	-2.7648	4.37E-12	4.19E-10	-6.92468	Down	collagen type I alpha 1 chain
STIM1-AS1	-2.76439	0.000124	0.000841	-3.83827	Down	STIM1 antisense RNA 1
APLP1	-2.76348	3.42E-17	1.12E-14	-8.43114	Down	amyloid beta precursor like protein 1
ARHGAP33	-2.73208	4.43E-17	1.42E-14	-8.4009	Down	Rho GTPase activating protein 33
DUOXA2	-2.72376	0.000224	0.001367	-3.69061	Down	dual oxidase maturation factor 2
ZNF839P1	-2.72326	0.001312	0.005816	-3.21335	Down	zinc finger protein 839 pseudogene 1
IGDCC3	-2.7068	3.17E-05	0.000275	-4.16094	Down	immunoglobulin superfamily DCC subclass member 3
HBA1	-2.70354	1.60E-08	4.74E-07	-5.65021	Down	hemoglobin subunit alpha 1
RTN4R	-2.70303	8.57E-12	7.72E-10	-6.82863	Down	reticulon 4 receptor
DOC2A	-2.68864	1.40E-07	2.97E-06	-5.26478	Down	double C2 domain alpha
PTPRVP	-2.68667	2.81E-05	0.000249	-4.18823	Down	protein tyrosine phosphatase receptor type V, pseudogene
TMEM121	-2.67382	1.20E-06	1.79E-05	-4.85638	Down	transmembrane protein 121
EPS8L2	-2.67091	1.78E-08	5.17E-07	-5.63197	Down	EPS8 like 2
CILP2	-2.66831	1.59E-05	0.000154	-4.31613	Down	cartilage intermediate layer protein 2
BCORP1	-2.66043	0.001467	0.006366	-3.18113	Down	BCL6 corepressor pseudogene 1
RIMBP2	-2.65867	0.001	0.004667	-3.29045	Down	RIMS binding protein 2
CA7	-2.65493	0.000783	0.00381	-3.35861	Down	carbonic anhydrase 7

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
FZD10-AS1	-2.65402	8.30E-06	9.09E-05	-4.45731	Down	FZD10 antisense divergent transcript
GNG8	-2.64512	0.001051	0.004859	-3.27649	Down	G protein subunit gamma 8
C10orf90	-2.63237	0.000445	0.002394	-3.51161	Down	chromosome 10 open reading frame 90
PALM3	-2.62953	0.001466	0.006363	-3.18132	Down	paralemmin 3
PPDPF	-2.62731	1.83E-10	1.07E-08	-6.37501	Down	pancreatic progenitor cell differentiation and proliferation factor
MTND6P24	-2.62664	0.01694	0.046233	-2.388	Down	MT-ND6 pseudogene 24
PRR12	-2.62536	1.14E-12	1.27E-10	-7.11302	Down	proline rich 12
ELFN1-AS1	-2.62504	0.000224	0.001368	-3.6904	Down	ELFN1 antisense RNA 1
GLI2	-2.6227	7.56E-16	1.87E-13	-8.06117	Down	GLI family zinc finger 2
OIT3	-2.61731	6.24E-05	0.000476	-4.00361	Down	oncprotein induced transcript 3
RP1L1	-2.60824	1.80E-07	3.68E-06	-5.21903	Down	RP1 like 1
C2CD4D	-2.60552	9.06E-05	0.000651	-3.91449	Down	C2 calcium-dependent domain containing 4D
SLC16A13	-2.60311	4.82E-09	1.67E-07	-5.85333	Down	solute carrier family 16 member 13
IER3-AS1	-2.59841	0.001292	0.005745	-3.21781	Down	IER3 antisense RNA 1
DUX4L26	-2.59701	0.002646	0.010262	-3.00617	Down	double homeobox 4 like 26 (pseudogene)
HMCN2	-2.59332	2.21E-13	2.94E-11	-7.33515	Down	hemicentin 2
R3HDML	-2.5901	0.011063	0.032856	-2.54069	Down	R3H domain containing like
KRTAP10-7	-2.58854	0.016217	0.044688	-2.40399	Down	keratin-associated protein 10-7
ATP6V1B1	-2.57882	0.000557	0.002881	-3.45183	Down	ATPase H+ transporting V1 subunit B1
NAT8L	-2.57001	3.28E-06	4.21E-05	-4.65255	Down	N-acetyltransferase 8 like
SRCIN1	-2.56661	9.07E-15	1.81E-12	-7.75162	Down	SRC kinase signaling inhibitor 1
NRGN	-2.56324	1.74E-08	5.07E-07	-5.63633	Down	neurogranin
PRKY	-2.56199	1.10E-08	3.41E-07	-5.71527	Down	protein kinase Y-linked (pseudogene)
GCSIR	-2.56155	0.000338	0.001919	-3.58443	Down	GPR55 cis regulatory suppressor of immune response RNA
TLCD3B	-2.55905	0.004609	0.016197	-2.83318	Down	TLC domain containing 3B
HBA2	-2.55637	1.02E-07	2.30E-06	-5.3224	Down	hemoglobin subunit alpha 2
THY1	-2.55521	9.72E-12	8.49E-10	-6.81066	Down	Thy-1 cell surface antigen
OFD1P8Y	-2.55452	0.004509	0.015917	-2.84018	Down	OFD1 pseudogene 8 Y-linked
RET	-2.55272	1.30E-14	2.44E-12	-7.70568	Down	ret proto-oncogene
CACNG8	-2.54658	1.41E-07	2.99E-06	-5.26385	Down	calcium voltage-gated channel auxiliary subunit gamma 8
FOXD3	-2.54645	0.000113	0.000783	-3.85981	Down	forkhead box D3
MAPK8IP1P1	-2.54579	0.014191	0.0401	-2.45239	Down	mitogen-activated protein kinase 8 interacting protein 1 pseudogene 1
STX1B	-2.54292	6.58E-13	7.98E-11	-7.18793	Down	syntaxin 1B
DBH	-2.54094	0.000237	0.001436	-3.67564	Down	dopamine beta-hydroxylase
GZMM	-2.52033	0.001709	0.007189	-3.13669	Down	granzyme M
CLDN5	-2.51806	2.10E-17	7.41E-15	-8.48797	Down	claudin 5
PPIAP39	-2.51602	0.00024	0.001448	-3.67281	Down	peptidylprolyl isomerase A pseudogene 39
AMBP	-2.51577	0.000259	0.00154	-3.65339	Down	alpha-1-microglobulin/bikunin precursor
IGF2	-2.51532	1.44E-08	4.32E-07	-5.66855	Down	insulin like growth factor 2
MXRAS5Y	-2.51245	1.69E-10	1.00E-08	-6.38708	Down	matrix remodeling-associated 5 Y-linked (pseudogene)
FOXP3	-2.51209	5.20E-05	0.00041	-4.04637	Down	forkhead box P3
GLP1R	-2.50999	2.54E-08	7.05E-07	-5.57025	Down	glucagon like peptide 1 receptor
ZNF683	-2.50826	0.001445	0.006294	-3.1855	Down	zinc finger protein 683
SYCE1	-2.5066	0.000828	0.003987	-3.34326	Down	synaptonemal complex central element protein 1
CYP2F1	-2.50653	6.04E-06	6.97E-05	-4.52515	Down	cytochrome P450 family 2 subfamily F member 1
LKAAEAR1	-2.50603	0.009467	0.028991	-2.59473	Down	LKAAEAR motif containing 1

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
TCF7L1	-2.50142	3.95E-12	3.83E-10	-6.93904	Down	transcription factor 7 like 1
SLC6A1-AS1	-2.48806	1.30E-09	5.65E-08	-6.06746	Down	SLC6A1 antisense RNA 1
NTN5	-2.48779	9.33E-06	9.97E-05	-4.43218	Down	netrin 5
DPRX	-2.48757	0.001582	0.006761	-3.15923	Down	divergent-paired related homeobox
MTND5P19	-2.48481	0.017196	0.046762	-2.38248	Down	MT-ND5 pseudogene 19
GYG2P1	-2.47504	3.22E-05	0.000278	-4.15758	Down	glycogenin 2 pseudogene 1
MTND2P12	-2.47088	0.004689	0.016426	-2.82765	Down	MT-ND2 pseudogene 12
SARDH	-2.46482	2.22E-09	8.81E-08	-5.98071	Down	sarcosine dehydrogenase
LYPD1	-2.45426	0.004416	0.015637	-2.84681	Down	LY6/PLAUR domain containing 1
L1TD1	-2.45214	0.010908	0.032464	-2.54564	Down	LINE1 type transposase domain containing 1
PRRT2	-2.45178	1.54E-13	2.16E-11	-7.38349	Down	proline rich transmembrane protein 2
SLC6A9	-2.44763	4.00E-16	1.06E-13	-8.13862	Down	solute carrier family 6 member 9
RNU6-321P	-2.44484	0.001516	0.00653	-3.17168	Down	RNA, U6 small nuclear 321, pseudogene
ACHE	-2.4389	2.27E-14	4.00E-12	-7.63413	Down	acetylcholinesterase (Cartwright blood group)
PNPLA7	-2.43362	2.02E-11	1.61E-09	-6.70477	Down	patatin-like phospholipase domain containing 7
C17orf50	-2.43052	0.010256	0.030877	-2.56708	Down	chromosome 17 open reading frame 50
IL34	-2.42559	3.58E-12	3.54E-10	-6.9529	Down	interleukin 34
CLIP3	-2.42499	1.84E-10	1.07E-08	-6.37395	Down	CAP-Gly domain containing linker protein 3
RNU1-31P	-2.41842	3.87E-06	4.81E-05	-4.61821	Down	RNA, U1 small nuclear 31, pseudogene
DEFB124	-2.41708	7.20E-05	0.000536	-3.96972	Down	defensin beta 124
TM7SF2	-2.41624	1.13E-37	5.82E-34	-12.8286	Down	transmembrane 7 superfamily member 2
ZSWIM9	-2.41143	1.75E-08	5.08E-07	-5.63547	Down	zinc finger SWIM-type containing 9
CTRB1	-2.41047	1.41E-05	0.00014	-4.34234	Down	chymotrypsinogen B1
PIK3R6	-2.40855	1.96E-15	4.45E-13	-7.94414	Down	phosphoinositide-3-kinase regulatory subunit 6
RNASE10	-2.40739	0.007658	0.024452	-2.66679	Down	ribonuclease A family member 10 (inactive)
NRXN2	-2.40499	2.03E-10	1.17E-08	-6.35874	Down	neurexin 2
TMPRSS6	-2.40366	0.000383	0.002127	-3.55145	Down	transmembrane serine protease 6
ZFXH2	-2.40102	5.30E-10	2.66E-08	-6.21001	Down	zinc finger homeobox 2
PODNL1	-2.39752	3.98E-07	7.12E-06	-5.06971	Down	podocan like 1
ADGRB1	-2.3927	2.63E-06	3.50E-05	-4.69758	Down	adhesion G protein-coupled receptor B1
C16orf78	-2.3906	0.000424	0.002303	-3.52469	Down	chromosome 16 open reading frame 78
MARGPRE	-2.38919	0.00096	0.004515	-3.30191	Down	MAS related GPR family member E
FIGNL2-DT	-2.38916	0.003786	0.013791	-2.8955	Down	FIGNL2 divergent transcript
SHANK1	-2.38796	4.81E-06	5.77E-05	-4.57295	Down	SH3 and multiple ankyrin repeat domains 1
GUCY1B2	-2.38687	0.000511	0.002683	-3.47483	Down	guanylatecyclase 1 soluble subunit beta 2 (pseudogene)
KCNN1	-2.38554	0.002291	0.009132	-3.04961	Down	potassium calcium-activated channel subfamily N member 1
NPPA	-2.3854	0.002748	0.010582	-2.99456	Down	natriuretic peptide A
MTCO3P22	-2.38323	0.008232	0.025929	-2.6424	Down	MT-CO3 pseudogene 22
UPK3BP1	-2.38283	7.41E-05	0.00055	-3.96272	Down	uroplakin 3B pseudogene 1
PHF21B	-2.38254	6.95E-06	7.85E-05	-4.49516	Down	PHD finger protein 21B
MLIP-IT1	-2.38121	0.003684	0.013469	-2.90399	Down	MLIP intronic transcript 1
UPK3B	-2.37776	1.96E-06	2.74E-05	-4.7574	Down	uroplakin 3B
UTS2R	-2.3705	0.002076	0.008412	-3.07916	Down	urotensin 2 receptor
PLPPR3	-2.36936	0.008809	0.027346	-2.61937	Down	phospholipid phosphatase related 3
DPYSL5	-2.36884	0.01321	0.037842	-2.47805	Down	dihydropyrimidinase like 5
C1QTNF9	-2.36667	3.11E-17	1.03E-14	-8.44223	Down	C1q and TNF related 9
MYCN	-2.36507	3.04E-08	8.14E-07	-5.53893	Down	MYCN proto-oncogene, bHLH transcription factor
IQCN	-2.36358	4.19E-14	6.64E-12	-7.55489	Down	IQ motif containing N

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
SYCE1L	-2.3627	0.000689	0.003442	-3.39388	Down	synaptonemal complex central element protein 1 like
FAM171A2	-2.36011	3.16E-06	4.08E-05	-4.66	Down	family with sequence similarity 171 member A2
ENTPD2	-2.35956	1.18E-09	5.17E-08	-6.08324	Down	ectonucleoside triphosphate diphosphohydrolase 2
BICDL2	-2.35952	0.004821	0.01679	-2.81877	Down	BICD family like cargo adaptor 2
LMTK3	-2.35747	9.81E-07	1.52E-05	-4.89548	Down	lemur tyrosine kinase 3
OGDHL	-2.35098	3.39E-13	4.36E-11	-7.27805	Down	oxoglutarate dehydrogenase L
OFD1P9Y	-2.35018	0.010683	0.03195	-2.55291	Down	OFD1 pseudogene 9 Y-linked
ZNF628	-2.34926	2.25E-08	6.32E-07	-5.5916	Down	zinc finger protein 628
PSD2	-2.34798	0.001056	0.004879	-3.27515	Down	pleckstrin and Sec7 domain containing 2
IL2RB	-2.34781	1.14E-09	5.05E-08	-6.08791	Down	interleukin 2 receptor subunit beta
ASGR1	-2.34753	0.004	0.014427	-2.87813	Down	asialoglycoprotein receptor 1
CCN1	-2.34567	1.08E-06	1.65E-05	-4.87672	Down	cellular communication network factor 1
KRT18P58	-2.34189	0.003655	0.013386	-2.90647	Down	keratin 18 pseudogene 58
TMEM132E	-2.34128	0.016615	0.04554	-2.39511	Down	transmembrane protein 132E
MTCO1P23	-2.33854	0.007951	0.025226	-2.65415	Down	MT-CO1 pseudogene 23
IGSF9	-2.33842	0.000443	0.002386	-3.51289	Down	immunoglobulin superfamily member 9
SLC5A2	-2.33461	1.86E-06	2.63E-05	-4.768	Down	solute carrier family 5 member 2
FRMD1	-2.33169	0.003686	0.013472	-2.90388	Down	FERM domain containing 1
TINCR	-2.33096	3.33E-05	0.000287	-4.14965	Down	TINCR ubiquitin domain containing
CROCCP4	-2.33006	0.000907	0.004304	-3.31779	Down	CROCC pseudogene 4
FIGNL2	-2.32742	2.97E-06	3.88E-05	-4.67274	Down	fidgetin like 2
CDSN	-2.32601	0.002325	0.009237	-3.04528	Down	corneodesmosin
RAB43	-2.32013	0.00016	0.00104	-3.77454	Down	RAB43, member RAS oncogene family
CACNA1G	-2.3186	1.19E-11	1.01E-09	-6.78111	Down	calcium voltage-gated channel subunit alpha1 G
SOX18	-2.31637	1.21E-06	1.82E-05	-4.85334	Down	SRY-box transcription factor 18
EFCC1	-2.31374	9.15E-12	8.14E-10	-6.81925	Down	EF-hand and coiled-coil domain containing 1
TMEM145	-2.31353	0.000263	0.00156	-3.64933	Down	transmembrane protein 145
ADRA2A	-2.31285	6.71E-09	2.22E-07	-5.79806	Down	adrenoceptor alpha 2A
P2RY8	-2.31022	7.12E-18	2.88E-15	-8.61294	Down	P2Y receptor family member 8
RPL18AP14	-2.30597	0.002898	0.011041	-2.97838	Down	ribosomal protein L18a pseudogene 14
KCNJ9	-2.30447	9.20E-05	0.000659	-3.91091	Down	potassium inwardly rectifying channel subfamily J member 9
PERCC1	-2.30111	0.00217	0.008717	-3.06597	Down	proline and glutamate rich with coiled coil 1
PANX2	-2.29938	0.004126	0.014809	-2.86836	Down	pannexin 2
ACOXL	-2.29881	0.000511	0.002681	-3.47501	Down	acyl-CoA oxidase like
MRPL12	-2.29849	5.75E-08	1.40E-06	-5.42656	Down	mitochondrial ribosomal protein L12
KCNF1	-2.2959	0.001876	0.007749	-3.10919	Down	potassium voltage-gated channel modifier subfamily F member 1
DUOX2	-2.29502	3.40E-10	1.81E-08	-6.27923	Down	dual oxidase 2
SNX19P4	-2.28619	2.92E-06	3.82E-05	-4.67642	Down	sorting nexin 19 pseudogene 4
BRSK1	-2.28322	5.23E-09	1.80E-07	-5.83973	Down	BR serine/threonine kinase 1
PSAT1P3	-2.28151	0.001777	0.007422	-3.12524	Down	phosphoserine aminotransferase 1 pseudogene 3
AQP12B	-2.28151	0.00146	0.006347	-3.18246	Down	aquaporin 12B
PDE4C	-2.27831	1.12E-06	1.69E-05	-4.86984	Down	phosphodiesterase 4C
CHERP	-2.27507	4.49E-10	2.30E-08	-6.23601	Down	calcium homeostasis endoplasmic reticulum protein
ARID5A	-2.27456	2.37E-11	1.84E-09	-6.68092	Down	AT-rich interaction domain 5A
COL20A1	-2.27281	0.007612	0.024328	-2.6688	Down	collagen type XX alpha 1 chain
FOXO6	-2.27206	9.53E-06	0.000102	-4.42747	Down	forkhead box O6

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
RSP02	-2.26961	0.006776	0.022115	-2.70767	Down	R-spondin 2
MXRA5	-2.26826	1.80E-10	1.06E-08	-6.37763	Down	matrix remodeling-associated 5
ETS1-AS1	-2.26747	4.32E-06	5.26E-05	-4.59557	Down	ETS1 antisense RNA 1
SEZ6L	-2.26711	1.34E-06	1.97E-05	-4.83439	Down	seizure related 6 homolog like
SLC34A3	-2.26426	8.79E-07	1.39E-05	-4.9169	Down	solute carrier family 34 member 3
ISLR2	-2.26368	7.31E-16	1.84E-13	-8.06518	Down	immunoglobulin superfamily containing leucine rich repeat 2
C1QTNF12	-2.25484	6.17E-05	0.000471	-4.0063	Down	C1q and TNF related 12
IQCA1	-2.25295	1.03E-10	6.51E-09	-6.46319	Down	IQ motif containing with AAA domain 1
TMEM59L	-2.25074	3.58E-06	4.53E-05	-4.63426	Down	transmembrane protein 59 like
LMNTD2	-2.24913	0.00123	0.005519	-3.23172	Down	lamin tail domain containing 2
SNORD37	-2.24319	0.001456	0.006328	-3.1834	Down	small nucleolar RNA, C/D box 37
B4GALNT4	-2.24123	7.74E-05	0.00057	-3.95225	Down	beta-1,4-N-acetyl-galactosaminyltransferase 4
OXER1	-2.23961	2.42E-09	9.45E-08	-5.96682	Down	oxoeicosanoid receptor 1
FBXL16	-2.23826	3.88E-07	6.97E-06	-5.07483	Down	F-box and leucine rich repeat protein 16
BGN	-2.23532	1.02E-09	4.59E-08	-6.10609	Down	biglycan
KLK10	-2.23502	0.003998	0.014424	-2.87829	Down	kallikrein related peptidase 10
NOS2	-2.23486	8.89E-08	2.04E-06	-5.34813	Down	nitric oxide synthase 2
SSPOP	-2.23408	7.10E-12	6.50E-10	-6.85557	Down	SCO-spondin, pseudogene
AGRN	-2.23361	2.43E-20	1.56E-17	-9.24168	Down	agrin
KCNC3	-2.22953	2.78E-08	7.59E-07	-5.55472	Down	potassium voltage-gated channel subfamily C member 3
RNU1-129P	-2.22634	0.013814	0.039221	-2.46205	Down	RNA, U1 small nuclear 129, pseudogene
MYO3B-AS1	-2.22206	0.006159	0.020437	-2.73918	Down	MYO3B antisense RNA 1
GP5	-2.22182	0.001462	0.006351	-3.18211	Down	glycoprotein V platelet
NXPH4	-2.22096	0.000762	0.00373	-3.36634	Down	neurexophilin 4
RN7SKP57	-2.22006	7.00E-05	0.000525	-3.97614	Down	RN7SK pseudogene 57
RHCG	-2.2183	0.013078	0.037549	-2.48164	Down	Rh family C glycoprotein
ILDR1	-2.21663	0.011963	0.035027	-2.51324	Down	immunoglobulin like domain containing receptor 1
DPPA2P1	-2.21463	0.004363	0.015485	-2.85061	Down	developmental pluripotency-associated 2 pseudogene 1
ATN1	-2.21455	1.28E-09	5.56E-08	-6.0702	Down	atrophin 1
TMEM240	-2.21328	5.50E-07	9.33E-06	-5.00791	Down	transmembrane protein 240
GABRD	-2.21257	0.000126	0.00085	-3.83465	Down	gamma-aminobutyric acid type A receptor subunit delta
TMPRSS9	-2.21056	1.76E-07	3.62E-06	-5.22295	Down	transmembrane serine protease 9
ERICH4	-2.20739	1.87E-09	7.61E-08	-6.0085	Down	glutamate rich 4
DUSP8	-2.20557	1.74E-13	2.39E-11	-7.36744	Down	dual specificity phosphatase 8
SEC1P	-2.20125	4.40E-05	0.00036	-4.08523	Down	secretory blood group 1, pseudogene
LRRRC36	-2.20092	0.006616	0.021682	-2.71556	Down	leucine rich repeat containing 36
LAMP5	-2.19636	0.004457	0.015761	-2.84389	Down	lysosomal-associated membrane protein family member 5
FOXN4	-2.1962	0.006671	0.021835	-2.71283	Down	forkhead box N4
PCGF2	-2.19263	7.89E-09	2.55E-07	-5.77072	Down	polycomb group ring finger 2
H3-4	-2.18887	0.008728	0.027143	-2.62253	Down	H3.4 histone
PRRG3	-2.18611	5.58E-10	2.78E-08	-6.20184	Down	proline rich and Gla domain 3
DRD1	-2.18589	0.013624	0.038814	-2.46704	Down	dopamine receptor D1
MAMSTR	-2.18365	5.31E-11	3.72E-09	-6.56199	Down	MEF2 activating motif and SAP domain containing transcriptional regulator
ANKRD24	-2.18362	9.58E-07	1.49E-05	-4.90012	Down	ankyrin repeat domain 24

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
BEGAIN	-2.18234	3.85E-10	2.00E-08	-6.25983	Down	brain enriched guanylate kinase associated
FOXI2	-2.18159	0.002899	0.011044	-2.97824	Down	forkhead box I2
RPL23AP66	-2.18022	0.003306	0.012312	-2.93771	Down	ribosomal protein L23a pseudogene 66
COL9A1	-2.18	2.87E-09	1.09E-07	-5.9391	Down	collagen type IX alpha 1 chain
KRTAP10-11	-2.17351	0.011701	0.034405	-2.52104	Down	keratin-associated protein 10-11
GRIK4	-2.16696	3.70E-05	0.000313	-4.12527	Down	glutamate ionotropic receptor kainate type subunit 4
BAALC-AS2	-2.16416	0.005768	0.019374	-2.76069	Down	BAALC antisense RNA 2
CCL3	-2.16136	0.000955	0.004498	-3.30341	Down	C-C motif chemokine ligand 3
COL11A2	-2.1607	2.66E-11	2.03E-09	-6.66427	Down	collagen type XI alpha 2 chain
RN7SL202P	-2.15989	0.005109	0.017562	-2.8001	Down	RNA, 7SL, cytoplasmic 202, pseudogene
LTBP4	-2.15753	1.25E-14	2.35E-12	-7.71093	Down	latent transforming growth factor beta binding protein 4
TRIM50	-2.1574	1.78E-06	2.53E-05	-4.77679	Down	tripartite motif containing 50
ADGRG5	-2.14625	7.15E-05	0.000533	-3.97109	Down	adhesion G protein-coupled receptor G5
SAMD11P1	-2.14455	9.60E-06	0.000102	-4.42592	Down	sterile alpha motif domain containing 11 pseudogene 1
SLC17A7	-2.13874	7.48E-10	3.56E-08	-6.1555	Down	solute carrier family 17 member 7
WHRN	-2.13771	7.30E-06	8.17E-05	-4.48489	Down	whirlin
MBD6	-2.13614	3.52E-09	1.29E-07	-5.90532	Down	methyl-CpG binding domain protein 6
ZNF414	-2.13232	2.39E-09	9.34E-08	-5.96896	Down	zinc finger protein 414
ISLR	-2.1306	2.62E-36	1.18E-32	-12.583	Down	immunoglobulin superfamily containing leucine rich repeat
KIF26B	-2.12741	7.13E-06	8.02E-05	-4.48968	Down	kinesin family member 26B
RFX1	-2.12674	3.57E-10	1.87E-08	-6.27188	Down	regulatory factor X1
SHANK2	-2.12333	1.93E-08	5.53E-07	-5.61843	Down	SH3 and multiple ankyrin repeat domains 2
TNFRSF18	-2.12084	0.01253	0.036332	-2.49686	Down	TNF receptor superfamily member 18
MRPS21P7	-2.12048	0.002107	0.008517	-3.07466	Down	mitochondrial ribosomal protein S21 pseudogene 7
RNU6-1306P	-2.12009	0.006834	0.022266	-2.70483	Down	RNA, U6 small nuclear 1306, pseudogene
MYH11	-2.11903	1.68E-09	6.98E-08	-6.02654	Down	myosin heavy chain 11
ADRA1D	-2.11595	0.000191	0.0012	-3.73117	Down	adrenoceptor alpha 1D
SCT	-2.11518	0.000784	0.00381	-3.35848	Down	secretin
ZNF469	-2.11477	1.93E-13	2.61E-11	-7.35371	Down	zinc finger protein 469
BIRC7	-2.11335	0.006668	0.021825	-2.713	Down	baculoviral IAP repeat containing 7
IQSEC3	-2.11314	1.33E-11	1.11E-09	-6.76538	Down	IQ motif and Sec7 domain ArfGEF 3
CDH23	-2.10915	9.84E-36	3.93E-32	-12.478	Down	cadherin related 23
SDSL	-2.10885	2.54E-11	1.96E-09	-6.67098	Down	serine dehydratase like
CECR3	-2.10827	0.000711	0.003532	-3.38514	Down	cat eye syndrome chromosome region, candidate 3
LTBP2	-2.10749	4.84E-08	1.21E-06	-5.45694	Down	latent transforming growth factor beta binding protein 2
KRTAP12-1	-2.10631	0.014011	0.039687	-2.45699	Down	keratin-associated protein 12-1
COMP	-2.10261	0.00359	0.013189	-2.91212	Down	cartilage oligomeric matrix protein
ARHGEF16	-2.10106	2.11E-06	2.90E-05	-4.74286	Down	Rho guanine nucleotide exchange factor 16
RASA4	-2.10077	1.08E-06	1.65E-05	-4.87636	Down	RAS p21 protein activator 4
CYP2W1	-2.0992	0.000428	0.002322	-3.52188	Down	cytochrome P450 family 2 subfamily W member 1
MSI1	-2.09799	5.68E-15	1.17E-12	-7.81086	Down	musashi RNA binding protein 1
PCDHA2	-2.08955	0.002206	0.008837	-3.06107	Down	protocadherin alpha 2
KIAA1210	-2.08779	7.13E-05	0.000532	-3.97194	Down	KIAA1210
SLC26A10	-2.08301	8.04E-08	1.87E-06	-5.36616	Down	solute carrier family 26 member 10

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
PRXL2AP1	-2.08172	0.008009	0.025359	-2.65169	Down	peroxiredoxin like 2A pseudogene 1
DNAAF3	-2.08085	8.79E-11	5.68E-09	-6.4865	Down	dynein axonemal assembly factor 3
HR	-2.07873	2.63E-07	5.05E-06	-5.1485	Down	HR lysine demethylase and nuclear receptor corepressor
SLC9A3P3	-2.07738	0.002318	0.009212	-3.04617	Down	solute carrier family 9 member 3 pseudogene 3
IL1RAPL2	-2.07354	8.07E-05	0.00059	-3.9424	Down	interleukin 1 receptor accessory protein like 2
SP2	-2.07256	4.94E-12	4.68E-10	-6.9074	Down	Sp2 transcription factor
KHSRPP1	-2.07131	0.005217	0.017862	-2.7933	Down	KH-type splicing regulatory protein pseudogene 1
IER3	-2.07119	4.97E-06	5.93E-05	-4.56595	Down	immediate early response 3
CRISPLD1	-2.07016	2.04E-08	5.82E-07	-5.60875	Down	cysteine rich secretory protein LCCL domain containing 1
F8A2	-2.06923	1.57E-05	0.000153	-4.31845	Down	coagulation factor VIII associated 2
PBX4	-2.06696	0.007316	0.02356	-2.68212	Down	PBX homeobox 4
MTND1P6	-2.06619	0.002189	0.00878	-3.06334	Down	MT-ND1 pseudogene 6
C10orf71	-2.0658	7.44E-21	5.04E-18	-9.36737	Down	chromosome 10 open reading frame 71
PRRT1B	-2.06053	0.000135	0.000899	-3.81775	Down	proline rich transmembrane protein 1B
EHD2	-2.06051	2.21E-11	1.75E-09	-6.69146	Down	EH domain containing 2
DCX	-2.05781	0.002866	0.010945	-2.98178	Down	doublecortin
KRTAP5-AS1	-2.05712	4.73E-05	0.000381	-4.06836	Down	KRTAP5-1/KRTAP5-2 antisense RNA 1
GNB3	-2.05583	2.26E-09	8.95E-08	-5.97759	Down	G protein subunit beta 3
DOCK6	-2.05447	1.93E-13	2.61E-11	-7.35371	Down	dedicator of cytokinesis 6
SLC4A11	-2.05006	3.15E-08	8.33E-07	-5.53309	Down	solute carrier family 4 member 11
ASIC1	-2.04668	5.01E-10	2.53E-08	-6.2187	Down	acid sensing ion channel subunit 1
PTGDS	-2.04612	3.04E-11	2.30E-09	-6.64459	Down	prostaglandin D2 synthase
SOD3	-2.04605	7.56E-08	1.78E-06	-5.37723	Down	superoxide dismutase 3
SLC6A1	-2.0448	5.66E-26	9.15E-23	-10.5398	Down	solute carrier family 6 member 1
KDM6B	-2.03993	3.62E-11	2.66E-09	-6.61885	Down	lysine demethylase 6B
OPCML	-2.03832	3.96E-13	4.99E-11	-7.25701	Down	opioid binding protein/cell adhesion molecule like
RXFP4	-2.0331	8.74E-05	0.000632	-3.92304	Down	relaxin family peptide/INSL5 receptor 4
DNM1P29	-2.02973	0.009965	0.03019	-2.57705	Down	dynamain 1 pseudogene 29
ZBTB12	-2.02859	4.33E-08	1.10E-06	-5.47684	Down	zinc finger and BTB domain containing 12
EGR2	-2.02834	3.61E-06	4.56E-05	-4.63271	Down	early growth response 2
AHDC1	-2.02789	1.25E-10	7.77E-09	-6.43363	Down	AT-hook DNA binding motif containing 1
MDK	-2.0266	2.50E-10	1.39E-08	-6.32692	Down	midkine
NOXA1	-2.02565	1.08E-06	1.65E-05	-4.8768	Down	NADPH oxidase activator 1
ZMYND15	-2.0256	4.21E-06	5.15E-05	-4.60055	Down	zinc finger MYND-type containing 15
WDR62	-2.02471	1.19E-08	3.68E-07	-5.70049	Down	WD repeat domain 62
NDUFB2-AS1	-2.02398	0.002752	0.010591	-2.99418	Down	NDUFB2 antisense RNA 1
LLPH-DT	-2.0236	0.000159	0.001036	-3.77597	Down	LLPH divergent transcript
TTBK1	-2.01969	4.45E-05	0.000363	-4.08255	Down	tau tubulin kinase 1
LTBP3	-2.01804	5.27E-17	1.62E-14	-8.38053	Down	latent transforming growth factor beta binding protein 3
NOTCH3	-2.01692	3.41E-13	4.37E-11	-7.27725	Down	notch receptor 3
RGS4	-2.01611	3.42E-06	4.35E-05	-4.64411	Down	regulator of G protein signaling 4
IGFN1	-2.01476	0.003933	0.01423	-2.88349	Down	immunoglobulin like and fibronectin type III domain containing 1
CCNHP1	-2.01377	0.008975	0.027774	-2.61301	Down	cyclin H pseudogene 1
DYRK1B	-2.01145	8.49E-12	7.67E-10	-6.83001	Down	dual specificity tyrosine phosphorylation regulated kinase 1B
GIPC3	-2.01129	2.45E-14	4.23E-12	-7.62456	Down	GIPC PDZ domain containing family member 3

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
TLL10	-2.00745	0.000338	0.001918	-3.58461	Down	tubulin tyrosine ligase like 10
KIAA1755	-2.00452	1.17E-14	2.23E-12	-7.71958	Down	KIAA1755
OXT	-2.00451	0.01498	0.041924	-2.43286	Down	oxytocin/neurophysin I prepropeptide
NR1D1	-2.0012	4.47E-08	1.13E-06	-5.47103	Down	nuclear receptor subfamily 1 group D member 1
LCN1P1	-2.00098	0.004434	0.015691	-2.84553	Down	lipocalin 1 pseudogene 1
AEBP1	-2.00076	4.08E-11	2.93E-09	-6.6012	Down	AE binding protein 1
DNM1P46	-1.99973	1.07E-07	2.39E-06	-5.3146	Down	dynamamin 1 pseudogene 46
KANK4	-1.99864	9.41E-06	0.0001	-4.4302	Down	KN motif and ankyrin repeat domains 4
PDZD7	-1.99656	0.000164	0.001057	-3.76925	Down	PDZ domain containing 7
S1PR5	-1.98781	0.000292	0.001699	-3.62228	Down	sphingosine-1-phosphate receptor 5
UNC80	-1.9843	0.000237	0.001436	-3.67566	Down	unc-80 homolog, NALCN channel complex subunit
CALML6	-1.98229	0.006138	0.020383	-2.74034	Down	calmodulin like 6
FSCN1	-1.98091	1.61E-10	9.59E-09	-6.39435	Down	fascin actin-bundling protein 1
SLC1A7	-1.9797	9.74E-12	8.49E-10	-6.81026	Down	solute carrier family 1 member 7
SPATA32	-1.97839	0.012148	0.035471	-2.50781	Down	spermatogenesis-associated 32
WNK2	-1.97507	2.93E-10	1.59E-08	-6.30238	Down	WNK lysine deficient protein kinase 2
KIR3DX1	-1.97437	0.008635	0.02693	-2.62616	Down	killer cell immunoglobulin like receptor, three Ig domains X1 (pseudogene)
ATCAY	-1.97351	1.32E-05	0.000133	-4.35701	Down	ATCAY kinesin light chain interacting caytaxin
SLC4A1	-1.97305	0.000749	0.003684	-3.37085	Down	solute carrier family 4 member 1 (Diego blood group)
PIANP	-1.97293	0.000497	0.002622	-3.48225	Down	PILR alpha-associated neural protein
CPLX1	-1.9726	1.56E-07	3.28E-06	-5.24485	Down	complexin 1
CDRT15P3	-1.97253	0.001858	0.007687	-3.11209	Down	CDRT15 pseudogene 3
FOXD2-AS1	-1.97222	0.000895	0.00426	-3.32152	Down	FOXD2 adjacent opposite strand RNA 1
LRR3	-1.97183	2.68E-09	1.03E-07	-5.95001	Down	leucine rich repeat containing 3
MN1	-1.97157	2.92E-21	2.18E-18	-9.46573	Down	MN1 proto-oncogene, transcriptional regulator
UPK2	-1.97049	0.01386	0.039335	-2.46088	Down	uroplakin 2
GAPDHP15	-1.97032	1.13E-05	0.000116	-4.39131	Down	glyceraldehyde-3-phosphate dehydrogenase pseudogene 15
LMX1B	-1.96935	7.79E-10	3.66E-08	-6.14925	Down	LIM homeobox transcription factor 1 beta
APCDD1L	-1.9693	2.02E-16	5.67E-14	-8.22085	Down	APC down-regulated 1 like
AZIN2	-1.96918	8.98E-16	2.20E-13	-8.04	Down	antizyme inhibitor 2
C16orf74	-1.96917	0.000488	0.00258	-3.48721	Down	chromosome 16 open reading frame 74
MTCO3P43	-1.969	0.001288	0.005728	-3.21874	Down	MT-CO3 pseudogene 43
P2RX2	-1.96722	0.00992	0.030076	-2.57862	Down	purinergic receptor P2X 2
TNNT3	-1.96705	4.10E-07	7.30E-06	-5.06427	Down	troponin T3, fast skeletal type
OASL	-1.96687	1.86E-09	7.57E-08	-6.00986	Down	2'-5'-oligoadenylate synthetase like
DBP	-1.96673	3.00E-08	8.05E-07	-5.54153	Down	D-box binding PAR bZIP transcription factor
SOX8	-1.96619	2.27E-06	3.08E-05	-4.72781	Down	SRY-box transcription factor 8
KIF26A	-1.96566	2.61E-15	5.69E-13	-7.9085	Down	kinesin family member 26A
CARNS1	-1.96474	8.26E-19	3.91E-16	-8.85639	Down	carnosine synthase 1
CCDC85B	-1.96323	3.13E-08	8.30E-07	-5.53427	Down	coiled-coil domain containing 85B
CDHR5	-1.9623	1.03E-07	2.31E-06	-5.32162	Down	cadherin related family member 5
SAMD11	-1.96228	6.09E-08	1.48E-06	-5.41623	Down	sterile alpha motif domain containing 11
BOC	-1.96112	2.02E-12	2.11E-10	-7.03318	Down	BOC cell adhesion associated, oncogene regulated
MGAT5B	-1.95866	0.005012	0.017313	-2.80623	Down	alpha-1,6-mannosylglycoprotein 6-beta-N-acetylglucosaminyltransferase B
IPO9-AS1	-1.95826	1.33E-05	0.000133	-4.35562	Down	IPO9 antisense RNA 1

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
CRTC1	-1.95752	1.80E-09	7.38E-08	-6.0146	Down	CREB regulated transcription coactivator 1
PNMA3	-1.95473	3.28E-05	0.000283	-4.1531	Down	PNMA family member 3
ADGRE3	-1.95424	0.000644	0.003263	-3.41233	Down	adhesion G protein-coupled receptor E3
RPL13AP11	-1.95296	7.13E-10	3.41E-08	-6.16312	Down	ribosomal protein L13a pseudogene 11
PRRT4	-1.95181	1.90E-05	0.000178	-4.27662	Down	proline rich transmembrane protein 4
BAHCC1	-1.95038	2.18E-11	1.73E-09	-6.6933	Down	BAH domain and coiled-coil containing 1
ESPNL	-1.95024	0.012811	0.036951	-2.48897	Down	espin like
LRRC43	-1.94951	3.10E-06	4.02E-05	-4.66393	Down	leucine rich repeat containing 43
RN7SL774P	-1.94769	0.011299	0.033429	-2.53331	Down	RNA, 7SL, cytoplasmic 774, pseudogene
KLK13	-1.94498	0.016512	0.045337	-2.39739	Down	kallikrein related peptidase 13
FOXS1	-1.94449	8.04E-09	2.59E-07	-5.76757	Down	forkhead box S1
CHAD	-1.94355	1.41E-05	0.00014	-4.34263	Down	chondroadherin
RNF224	-1.94175	0.001586	0.00677	-3.15848	Down	ring finger protein 224
TMEM18-DT	-1.93908	0.014914	0.041773	-2.43446	Down	TMEM18 divergent transcript
TP63	-1.93803	6.80E-12	6.24E-10	-6.86174	Down	tumor protein p63
IGHEP2	-1.93791	3.55E-06	4.49E-05	-4.63634	Down	immunoglobulin heavy constant epsilon P2 (pseudogene)
CDH3	-1.93534	0.000213	0.001317	-3.7029	Down	cadherin 3
FBXO39	-1.9351	4.82E-05	0.000386	-4.06399	Down	F-box protein 39
EGR3	-1.93493	0.000255	0.001523	-3.65671	Down	early growth response 3
TBX21	-1.93015	0.001107	0.005069	-3.26176	Down	T-box transcription factor 21
LRCOL1	-1.92831	0.005781	0.019399	-2.75997	Down	leucine rich colipase like 1
CCDC120	-1.92827	2.62E-09	1.01E-07	-5.9536	Down	coiled-coil domain containing 120
EPPK1	-1.92743	1.46E-05	0.000144	-4.33391	Down	epiplakin 1
RHPN1	-1.92522	1.44E-06	2.10E-05	-4.81921	Down	rhophilin Rho GTPase binding protein 1
ERFL	-1.92385	0.000573	0.002955	-3.44394	Down	ETS repressor factor like
SBK2	-1.92338	0.001966	0.008042	-3.09525	Down	SH3 domain binding kinase family member 2
NOTCH1	-1.92318	1.21E-09	5.30E-08	-6.07852	Down	notch receptor 1
TMEM86B	-1.92194	9.00E-05	0.000648	-3.91598	Down	transmembrane protein 86B
CACNA1S	-1.92186	0.005317	0.018156	-2.78719	Down	calcium voltage-gated channel subunit alpha1 S
LOXL2	-1.91923	5.44E-10	2.72E-08	-6.20586	Down	lysyl oxidase like 2
KLHL38	-1.91876	7.33E-11	4.94E-09	-6.51365	Down	kelch-like family member 38
GATA1	-1.91777	0.008277	0.026021	-2.64056	Down	GATA binding protein 1
COL5A1	-1.91427	1.88E-13	2.56E-11	-7.3574	Down	collagen type V alpha 1 chain
CASKIN1	-1.91056	8.88E-06	9.58E-05	-4.44273	Down	CASK interacting protein 1
KCNK7	-1.91023	1.76E-07	3.62E-06	-5.223	Down	potassium two pore domain channel subfamily K member 7
OR10V3P	-1.90801	0.009463	0.028988	-2.59485	Down	olfactory receptor family 10 subfamily V member 3 pseudogene
ZFY	-1.90697	0.001128	0.005146	-3.25645	Down	zinc finger protein Y-linked
COL9A2	-1.90528	1.49E-06	2.16E-05	-4.81317	Down	collagen type IX alpha 2 chain
SPDYE7P	-1.9051	3.68E-07	6.68E-06	-5.08492	Down	speedy/RINGO cell cycle regulator family member E7, pseudogene
MTCO3P16	-1.90379	0.006171	0.02046	-2.73856	Down	MT-CO3 pseudogene 16
ADGRF1	-1.90155	0.010333	0.031067	-2.56448	Down	adhesion G protein-coupled receptor F1
CBARP	-1.90116	0.000417	0.002276	-3.52883	Down	CACN subunit beta-associated regulatory protein
DLGAP4	-1.90101	9.12E-13	1.06E-10	-7.14311	Down	DLG-associated protein 4
WNT10B	-1.89834	0.000179	0.001142	-3.74657	Down	Wnt family member 10B
PRKX-AS1	-1.89728	0.000186	0.001174	-3.73771	Down	PRKX antisense RNA 1
LRRC37A11P	-1.89707	7.15E-05	0.000533	-3.97133	Down	leucine rich repeat containing 37 member A11, pseudogene

Table 1 (continued)

Gene Symbol	logFC	P Value	adj. P.Vcal	T value	Regulation	Gene name
MRC2	-1.89563	3.92E-13	4.97E-11	-7.25814	Down	mannose receptor C type 2
CCNP	-1.89354	0.017941	0.048399	-2.36683	Down	cyclin P
SLC25A6P4	-1.8922	0.002428	0.009588	-3.03212	Down	solute carrier family 25 member 6 pseudogene 4

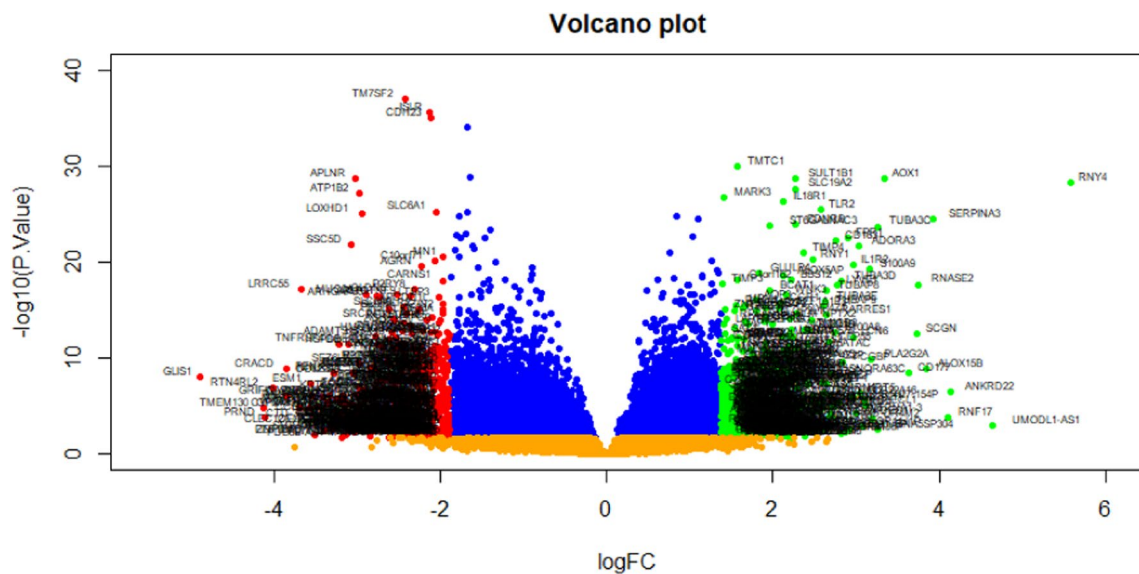


Fig. 1 Volcano plot of differentially expressed genes. Genes with a significant change of more than twofold were selected. Green dot represents up-regulated significant genes, and red dot represents down-regulated significant genes

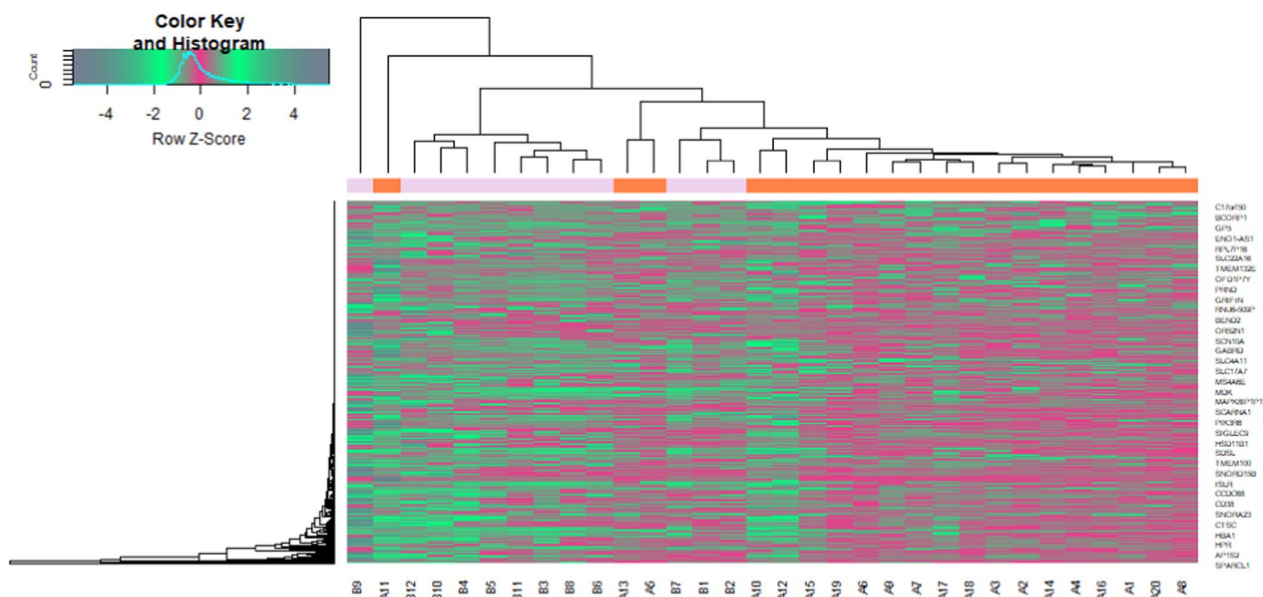


Fig. 2 Heat map of differentially expressed genes. Legend on the top left indicates log-fold change of genes. (A1–A20 = MI samples; B1–B12 = normal control samples)

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

GO ID	CATEGORY	GO Name	Adjusted p value	negative log10 of adjusted p value	Gene Count	Gene
Up-regulated genes						
GO:0050896	BP	response to stimulus	4.9346E-05	4.30674763	213	IL1RL1,SERPINA3,ALOX15B,RNASE2,CD177,VSIG4,OR4M2,PLA2G2A,S100A9,ADORA3,IL1R2,FPR1,CCL20,DEFB1,MT1A,LYVE1,CD163,S100A8,MCEMP1,ADAMDEC1,OR52N5,S100A12,CEP55,PPEF1,MMRN1,IgLV8-61,FAM83B,MTRNR2L11,TLR2,EDN2,PTPRQ,NPTX2,HAS2,PTX3,TMIGD3,IgLV5-45,TIMP4,CLEC4D,PKHD1,MT1X,AREG,MTRNR2L1,BMP3,FCGR1A,IgKV1D-8,EDNRB,FGF10,SULT1B1,RNF175,SIGLEC10,MUC16,SYT13,GCKR,BLM,CLEC4E,CCL23,LILRA5,OR13A1,MGST1,SERPINA5,WNK3,CAMP,SP1,SLC11A1,LBP,IL18R1,ALOX5AP,DLGAP5,TRPM1,H3C7,SPINK1,RETN,KNG1,CCR1,AKR1B10,IgKV2D-40,SLA,MYOT,TLR8,FCGR3A,PKHD1L1,TAS2R7,SHISA3,F13A1,H4C13,FCGR1B,EPCAM,CR1L,CATSPERB,GLUL,CXCL11,CLEC1B,CD53,MR1,TFRC,NAMPT,BIRC3,FPR2,SAA1,CCL26,FCN3,H2BC10,SLC30A10,KMO,AGTR1,TMEM100,GPR84,P2RY12,AQP3,FLT3,ADGRF4,TFEC,HPR,OR52N1,SIGLEC5,SIGLEC7,RAB39A,MSR1,TTK,SRGN,IgKV1-9,GPR151,GPR34,SAMSN1,TREML4,SLAMF8,MCTP2,AQP4,FCER1G,SIGLEC9,NQO1,MELK,CR1,LGR5,TREM2,CCL18,TRHDE,HP,TAS2R8,IRAK3,LY96,CCDC68,OXGR1,BATF,CYBB,RPL39,CDK1,RIDA,SLC7A11,H3C12,CTH,TOP2A,H3C8,CARD18,RHOU,CFTR,H2BC11,H4C6,TAS2R9,CLEC7A,F8,FKBP5,CTSC,MROH2B,JCHAIN,SLC17A3,C3AR1,TDGF1,SPARCL1,IgHV3-48,CCN6,ANKRD2,MYO16,CHL1,HIGD1A,CD38,RNASE6,RAD9B,CD180,MAOA,STC1,RPL26,RPS15A,BMPR1B,IgHV3-53,SLPI,SNX10,SERPINF2,APOB,KCNK2,FGF7,RGCC,GRB14,CALCRL,PRDX1,CMTM5,GPR12,ANGPTL1,LCP1,HPSE,LAPTMS,MARK3,TNFRSF11A,EEF1E1,IL18RAP,CLEC12A,PDE7A,TIMP3,EMB,PDE4D,C7,SHC4,DEPDC1B

Table 2 (continued)

GO ID	CATEGORY	GO Name	Adjusted p value	negative log10 of adjusted p value	Gene Count	Gene
GO:0007154	BP	cell communication	0.006449939	2.190444375	155	IL1RL1,ALOX15B,SCGN,CD177,OR4M2,PLA2G2A,S100A9,ADORA3,IL1R2,FPR1,CCL20,DEFB1,S100A8,OR52N5,S100A12,CEP55,PPEF1,FAM83B,MTRNR2L11,TLR2,EDN2,NPTX2,TMIGD3,TIMP4,CLEC4D,PKHD1,AREG,MTRNR2L1,BMP3,FCGR1A,EDNRB,FGF10,RNF175,MUC16,SYT13,BLM,CLEC4E,CCL23,LILRA5,OR13A1,WNK3,SPP1,LBP,IL18R1,DLGAP5,TRPM1,SCN10A,H3C7,SPINK1,RETN,KNG1,CCR1,IGKV2D-40,SLA,TLR8,FCGR3A,TAS2R7,SHISA3,F13A1,FCGR1B,EPCAM,GLUL,CXCL11,CLEC1B,CD53,TFRC,NAMPT,BIRC3,FPR2,SAA1,CCL26,SLC30A10,KMO,AGTR1,TMEM100,GPR84,P2RY12,AQP3,FLT3,ADGRF4,OR52N1,RAB39A,TTK,SRGN,GPR151,GPR34,TREML4,MCTP2,FCER1G,SIGLEC9,NQO1,MELK,CR1,LGR5,TREM2,CCL18,TRHDE,TAS2R8,IRAK3,LY96,CCDC68,OXGR1,BATF,CYBB,CDK1,SLC7A11,SYN2,H3C12,CTH,H3C8,RHOU,CFTR,H2BC11,TAS2R9,CLEC7A,CTSC,MROH2B,C3AR1,TDGF1,SPARCL1,IGHV3-48,CCN6,MYO16,CHL1,CD38,RAD9B,CD180,MAOA,STC1,RPL26,BMPR1B,IJGHV3-53,SERPINF2,APOB,KCNK2,FGF7,RCGC,GRB14,CALCRL,PRDX1,CMTM5,GPR12,ANGPTL1,LCP1,HPSE,LAPTM5,MARK3,TNFRSF11A,EEF1E1,IL18RAP,PDE7A,TIMP3,PDE4D,SHC4,DEPDC1B
GO:0071944	CC	cell periphery	1.36E-09	8.867810114	170	IL1RL1,SERPINA3,ALOX15B,CD177,OR4M2,PLA2G2A,S100A9,CLECL1,ADORA3,IL1R2,SLC22A16,FPR1,LYVE1,CD163,S100A8,MCEMP1,ADAMDEC1,OR52N5,S100A12,CEP55,MMRN1,IGLV8-61,TLR2,PTPRQ,DMMP1,ADH1B,HAS2,PTX3,TMIGD3,IGLV5-45,TIMP4,CLEC4D,PKHD1,FCGR1A,IGKV1D-8,EDNRB,SLC19A2,FGF10,RHAG,SIGLEC10,MUC16,SYT13,CLEC4E,LILRA5,OR13A1,MGST1,SERPINA5,SLCO4A1,CYP4A11,SLC11A1,IL18R1,TRPM1,MS4A4A,SCN10A,KNG1,CCR1,CSTA,IGKV2D-40,SLA,MYO10,ADH1A,TLR8,FCGR3A,PKHD1L1,SIGLEC12,TAS2R7,F13A1,CDH19,FCGR1B,EPCAM,CATSPERB,GLUL,CLEC1B,CD53,OTOG,LMRC1,TFRC,NAMPT,CPM,FPR2,ADH1C,FCN3,SLC30A10,AGTR1,LRRN3,TMEM100,GPR84,P2RY12,AQP3,FLT3,OR52N1,SIGLEC5,SIGLEC7,RAB39A,MSR1,IGKV1-9,GPR151,GPR34,PRRG4,TREML4,S100A3,CADM2,AQP4,FCER1G,SIGLEC9,MELK,CR1,LGR5,TREM2,TRHDE,TAS2R8,IRAK3,LY96,OXGR1,CYBB,KCNH7,SLC7A11,SIRPB2,SYN2,DSPP,RHOU,CFTR,H2BC11,CNTN3,TAS2R9,CLEC7A,UAP1,F8,CTSC,CATIP,SLC17A3,C3AR1,TDGF1,SMIM9,SPARCL1,IGHV3-48,CCN6,MYO16,XK,CHL1,CDCP1,CD38,CD180,STC1,BMPR1B,IJGHV3-53,SLPI,SERPINF2,APOB,KCNK2,GRB14,CALCRL,SDR16C5,GPR12,ANGPTL1,LCP1,HPSE,LAPTM5,MARK3,KIF20A,TMEM97,TNFRSF11A,IL18RAP,CLEC12A,TIMP3,EMB,AP1S2,PDE4D,C7,SHC4

Table 2 (continued)

GO ID	CATEGORY	GO Name	Adjusted p value	negative log10 of adjusted p value	Gene Count	Gene
GO:0016020	CC	membrane	2.24211E-06	5.649343059	223	IL1RL1,ALOX15B,SCGN,CD177,VSIG4,OR4M2,PLA2G2A,S100A9,CLECL1,KRT5,ADORA3,IL1R2,SLC22A16,FPR1,DEFB1,LYVE1,CD163,S100A8,MCEMP1,OR52N5,S100A12,CEP55,RARRES1,IGLV8-61,FAM83B,TLR2,PTPRQ,ADH1B,SLC25A48,HAS2,CYP4B1,TMIGD3,IGLV5-45,CLEC4D,PKHD1,AREG,FCGR1A,CYP4Z1,IGKV1D-8,EDNRB,SLC19A2,FGF10,RNF175,RHAG,SIGLEC10,MUC16,SYT13,CLEC4E,LILRA5,OR13A1,MGST1,SERPINA5,SLCO4A1,CYP4A11,SLC11A1,LBPJL18R1,ALOX5A,PTPRM1,MS4A4A,SCN10A,H3C7,KNG1,CCR1,CSTA,IGKV2D-40,SLA,MYOT,ADH1A,GALNTL6,CYP4A22,TLR8,FCGR3A,PKHD1L1,SIGLEC12,TAS2R7,SHISA3,CDH19,H4C13,FCGR1B,EPCAM,CR1L,CATSPERB,GLUL,CLEC1B,ST6GALNAC3,TIMD4,DHRS7C,CD53,TFCP2L1,MRC1,TFRC,NAMPT,CPM,BIRC3,FPR2,ADH1C,SLC30A10,KMO,AGTR1,STRIT1,LRN3,TMEM100,CHST9,GPR84,P2RY12,AQP3,FLT3,ADGRF4,OR52N1,SIGLEC5,HSD11B1,SIGLEC7,RAB39A,MSR1,TTK,IGKV1-9,GPR151,GPR34,PRRG4,TMPRSS12,TREML4,S100A3,CADM2,SLAMF8,MCTP2,AQP4,FCE R1G,SIGLEC9,HS6ST2,MELK,CR1,LGR5,TR EM2,TRHDE,TAS2R8,IRAK3,MANEA,LY96,MS4A6A,OXGR1,CYBB,KCNH7,CDK1,SGPP2,SLC7A11,SIRPB2,NDUFA4,TMTC1,SYN2,H3C12,C1ORF162,STARD7,H3C8,PLA1A,RHOU,CFTR,H2BC11,H4C6,CNTN3,TA S2R9,CLEC7A,UAP1,F8,FKBP5,CTSC,CATIPR PS29,SLC17A3,C3AR1,ATP5MD,TOMM20L,TDGF1,SMIM9,IGHV3-48,MRPS36,MYO16,XK,CHL1,CDCP1,HIGD1A,CD38,CD180,MAO A,STC1,RPL26,RPS15A,COX7A2,COX7B,BM PR1B,OSTC,IGHV3-53,TMEM126A,SNX10,A POB,KCNK2,GRB14,CALCRL,SDR16C5,CMT M5,GPR12,TMEM258,LCP1,HPSE,MS4A6E,L APTM5,RPS13,MARK3,KIF20A,TMEM97,GALNT15,TNFRSF11A,EEF1E1,UGT2B4,IL18RAP,MRPL50,CLEC12A,EMB,AP1S2,PDE4D,CYP4X1,C7,SHC4
GO:0060089	MF	molecular transducer activity	0.000421239	3.375471183	51	IL1RL1,OR4M2,ADORA3,IL1R2,FPR1,LYVE1,OR52N5,TLR2,TMIGD3,PKHD1,FCGR1A,EDNRB,CLEC4E,OR13A1,IL18R1,CCR1,MYOT,TLR8,FCGR3A,PKHD1L1,TAS2R7,FCGR1B,CLEC1B,MRC1,FPR2,AGTR1,GPR84,P2RY12,FLT3,ADGRF4,OR52N1,SIGLEC7,GPR151,GPR34,TR EML4,SLAMF8,FCER1G,CR1,LGR5,TREM2,TA S2R8,LY96,OXGR1,TAS2R9,CLEC7A,C3AR1,B MPR1B,CALCRL,GPR12,TNFRSF11A,IL18RAP
GO:0004888	MF	transmembrane signaling receptor activity	0.001403098	2.852912115	43	IL1RL1,OR4M2,ADORA3,IL1R2,FPR1,LYVE1,OR52N5,TLR2,TMIGD3,FCGR1A,EDNRB,OR13A1,IL18R1,CCR1,MYOT,TLR8,FCGR3A,TA S2R7,FCGR1B,CLEC1B,MRC1,FPR2,AGTR1, GPR84,P2RY12,FLT3,ADGRF4,OR52N1,GPR151,GPR34,FCER1G,CR1,LGR5,TREM2,TAS2R8,OXGR1,TAS2R9,C3AR1,BMPR1B,CALCRL,GPR12,TNFRSF11A,IL18RAP

Table 2 (continued)

GO ID	CATEGORY	GO Name	Adjusted p value	negative log10 of adjusted p value	Gene Count	Gene
Down-regulated genes						
GO:0032501	BP	multicellular organismal process	0.002147964	2.667973087	186	GLIS1,RTN4RL2,CRACD,ESM1,ACE,CELA2A,LY6H,PENK,TNFRSF4,CTRB2,KNDC1,OMPH,SPB6,SSC5D,AMH,COL22A1,LRFN1,TRPM5,APLNR,DDX3Y,CHD5,FOSB,ATP1B2,SEZ6L2,LOXHD1,DKKL1,TLR9,BARHL1,KRTAP5-1,TRIL,NXNL1,RSPH6A,SFRP4,ACER1,EGR1,MAST1,ESPN,CCDC63,COL1A1,APLP1,ARHGAP33,IGDCC3,RTN4R,DOC2A,EP58L2,GNG8,PPDPF,GLI2,RP1L1,KRTAP10-7,ATP6V1B1,SRGIN1,NRGN,THY1,RET,CACNG8,FOX3,STX1B,DBH,CLDN5,AMB,IGF2,FOXP3,GLP1R,ZNF683,NTN5,PRRT2,SLC6A9,ACHE,IL34,DEFB124,CTRB1,PIK3R6,NRXN2,ZFH2,ADGRB1,SHANK1,NPPA,UTS2R,DPYSL5,ENTPD2,ZNF628,CCN1,TMEM132E,IGSF9,CDSN,CACNA1G,SOX18,ADRA2A,PERCC1,PANX2,DUOX2,BRSK1,CHERP,FOXO6,RSPO2,ISLR2,BGN,NOS2-1,AGRN,GP5,ATN1,GABRD,FOXN4,PCGF2,DRD1,BEGAIN,COL9A1,KRTAP10-11,CCL3,COL11A2,LTBP4,SLC17A7,WHRN,KIF26B,SHANK2,TNFRSF18,MYH11,ADRA1D,SCT,BIRC7,CDH23,KRTAP12-1,COMP,MSI1,PCDHA2,IL1RAPL2,SP2,PBX4,EHD2,DCX,GNB3,DOC6,ASIC1,SLC6A1,KDM6B,OPCML,EGR2,MDK,ZMYND15,WDR62,TTBK1,LTBP3,NOTCH3,RGS4,IGFN1,DYRK1B,OXTR,NR1D1,PDZD7,S1PR5,SPATA32,ATCAY,SLC4A1,MN1,UPK2,LMX1B,AZIN2,P2RX2,TNNT3,DBP,SOX8,KIF26A,BOC,CRTC1,ESPNL,KLK13,FOX13,CHAD,TP63,CDH3,EGR3,TBX21,LRCOL1,CCDC120,EPPK1,NOTCH1,CACNA1S,LOXL2,GATA1,COL5A1,COL9A2,ADGRF1,DLGAP4,WNT10B,MRC2
GO:0048856	BP	anatomical structure development	0.005847965	2.232995209	148	RTN4RL2,ESM1,ACE,FBN3,CELA2A,LY6H,PENK,KNDC1,OMPH,SPB6,SSC5D,AMH,COL22A1,LRFN1,APLNR,CHD5,ATP1B2,SEZ6L2,DKKL1,TLR9,BARHL1,KRTAP5-1,RSPH6A,SFRP4,ACER1,EGR1,MAST1,CCDC63,COL1A1,APLP1,ARHGAP33,RTN4R,DOC2A,GNG8,PPDPF,GLI2,RP1L1,KRTAP10-7,ATP6V1B1,SRGIN1,NRGN,THY1,RET,FOX3,STX1B,CLDN5,IGF2,FOXP3,ZNF683,NTN5,ACHE,IL34,PIK3R6,NRXN2,ZFH2,ADGRB1,SHANK1,NPPA,DPYSL5,CCN1,TMEM132E,IGSF9,CDSN,SOX18,PERCC1,DUOX2,BRSK1,CHERP,FOXO6,RSPO2,ISLR2,BGN,AGRN,RHCG,ATN1,FOXN4,PCGF2,DRD1,MAMSTR,FOX12,COL9A1,KRTAP10-11,CCL3,COL11A2,LTBP4,SLC17A7,WHRN,KIF26B,SHANK2,TNFRSF18,MYH11,SCT,BIRC7,CDH23,KRTAP12-1,COMP,MSI1,PCDHA2,IL1RAPL2,IERS3,CRISPLD1,PBX4,EHD2,DCX,KDM6B,OPCML,EGR2,MDK,ZMYND15,WDR62,TTBK1,LTBP3,NOTCH3,RGS4,IGFN1,DYRK1B,OXTR,NR1D1,PDZD7,S1PR5,ATCAY,SLC4A1,MN1,UPK2,LMX1B,P2RX2,TNNT3,DBP,SOX8,KIF26A,BOC,CRTC1,KLK13,FOX13,CHAD,TP63,CDH3,EGR3,TBX21,CCDC120,EPPK1,NOTCH1,LOXL2,GATA1,COL5A1,COL9A2,ADGRF1,WNT10B

Table 2 (continued)

GO ID	CATEGORY	GO Name	Adjusted p value	negative log10 of adjusted p value	Gene Count	Gene
GO:0071944	CC	cell periphery	9.01283E-06	5.045138949	161	TMEM130,PRND,RTN4RL2,GPR78,LRRC55,ACE,FBN3,LY6H,PENK,TNFRSF4,SYT12,SLC7A4,MUC12,SSCS5,COL22A1,LRFN1,TRPM5,APLNR,ATP1B2,SEZ6L2,TLR9,MUC3A,ENTPD8,TRIL,LRRC38,MUC5B,GRID2IP,MAST1,ADAMTS14,COL1A1,APLP1,ARHGAP33,DUOXA2,IGDCC3,RTN4R,EP8L2,RIMBP2,GNG8,C10ORF90,PALM3,SLC16A13,HMCN2,ATP6V1B1,NRGN,THY1,RET,CACNG8,STX1B,CLDN5,AMBPG,LP1R,SYCE1,NTN5,LYPD1,PRRT2,SLC6A9,ACHE,CLIP3,TM7SF2,PIK3R6,NRXN2,TMPRSS6,PODNL1,ADGRB1,MRGPRE,SHANK1,KCNN1,NPPA,UPK3B,UTS2R,PLPPR3,ENTPD2,PSD2,IL2RB,ASGR1,CCN1,IGSF9,SLC5A2,FRMD1,CACNA1G,ADRA2A,P2RY8,KCNJ9,PANX2,KCNF1,DUOX2,COL20A1,MXRA5,SLC34A3,ISLR2,OXER1,BGN,NOS2,AGRN,KCNC3,GP5,RHCG,ILDR1,TMEM240,GABRD,TMPRSS9,LAMP5,DRD1,COL9A1,GRIK4,COL11A2,LTBP4,ADGRG5,SLC17A7,WHRN,SHANK2,TNFRSF18,ADRA1D,CDH23,LTBP2,COMP,RASA4,CYP2W1,PCDHA2,IL1RAPL2,EHD2,GNB3,SLC4A11,ASIC1,SOD3,SLC6A1,OPCML,RXFP4,MDK,NOXA1,LTBP3,NOTCH3,RGS4,AEBP1,PDZD7,S1PR5,UNC80,FSCN1,SLC1A7,WNK2,SLC4A1,PIANP,UPK2,APCDD1L,P2RX2,CDHR5,BOC,CRTC1,ADGRE3,CHAD,CDH3,EPPK1,NOTCH1,CACNA1S,LOXL2,COL5A1,KCNK7,COL9A2,ADGRF1,CBARP,DLGAP4
GO:0005886	CC	plasma membrane	0.005336788	2.272720017	136	TMEM130,PRND,RTN4RL2,GPR78,LRRC55,ACE,LY6H,PENK,TNFRSF4,SYT12,SLC7A4,MUC12,LRFN1,TRPM5,APLNR,ATP1B2,SEZ6L2,TLR9,MUC3A,ENTPD8,LRRC38,MUC5B,GRID2IP,MAST1,APLP1,ARHGAP33,DUOXA2,IGDCC3,RTN4R,EP8L2,RIMBP2,GNG8,C10ORF90,PALM3,SLC16A13,HMCN2,ATP6V1B1,NRGN,THY1,RET,CACNG8,STX1B,CLDN5,AMBPG,LP1R,SYCE1,LYPD1,PRRT2,SLC6A9,ACHE,CLIP3,TM7SF2,PIK3R6,NRXN2,TMPRSS6,ADGRB1,MRGPRE,SHANK1,KCNN1,UPK3B,UTS2R,PLPPR3,ENTPD2,PSD2,IL2RB,ASGR1,IGSF9,SLC5A2,FRMD1,CACNA1G,ADRA2A,P2RY8,KCNJ9,PANX2,KCNF1,DUOX2,SLC34A3,ISLR2,OXER1,BGN,NOS2,AGRN,KCNC3,GP5,RHCG,ILDR1,TMEM240,GABRD,TMPRSS9,LAMP5,DRD1,GRIK4,ADGRG5,SLC17A7,WHRN,SHANK2,TNFRSF18,ADRA1D,CDH23,RASA4,CYP2W1,PCDHA2,IL1RAPL2,EHD2,GNB3,SLC4A11,ASIC1,SLC6A1,OPCML,RXFP4,NOXA1,NOTCH3,RGS4,PDZD7,S1PR5,UNC80,FSCN1,SLC1A7,WNK2,SLC4A1,PIANP,UPK2,APCDD1L,P2RX2,CDHR5,BOC,CRTC1,ADGRE3,CDH3,EPPK1,NOTCH1,CACNA1S,KCNK7,ADGRF1,CBARP,DLGAP4
GO:0015318	MF	inorganic molecular entity transmembrane transporter activity	0.058426335	1.233391358	29	LRRC55,SLC7A4,TRPM5,ATP1B2,LRRC38,SLC16A13,ATP6V1B1,CACNG8,SLC6A9,KCNN1,SLC5A2,CACNA1G,KCNJ9,KCNF1,SLC34A3,KCNC3,RHCG,GABRD,GRIK4,SLC17A7,SLC4A11,ASIC1,SLC6A1,UNC80,SLC1A7,SLC4A1,P2RX2,CACNA1S,KCNK7

Table 2 (continued)

GO ID	CATEGORY	GO Name	Adjusted p value	negative log10 of adjusted p value	Gene Count	Gene
GO:0005198	MF	structural molecule activity	0.094978184	1.02237614	24	FBN3,HSPB6,COL22A1,MUC3A,COL1A1,OIT3,HMCN2,CLDN5,CCN1,PANX2,MRPL12,MXRA5,BGN,AGRN,COL9A1,COL11A2,LTBP4,MYH11,LTBP2,COMP,AEBP1,EPPK1,COL5A1,COL9A2

selected algorithms, including node degree, betweenness, stress and closeness. Finally, we identified ten hub genes (*cftr*, *cdk1*, *rps13*, *rps15a*, *rps27*, *notch1*, *mrpl12*, *nos2*, *ccdc85b* and *atn1*) and are listed Table 4. Then, the significant modules were identified via the PEWCC1 plugin. The top two significant modules were selected. The functional enrichment analysis of genes in module 1 and module 2 were conducted by g:Profiler. Module 1 consisted of 59 nodes and 203 edges (Fig. 4A). Hub genes in module 1 were significantly enriched in metabolism of amino acids and derivatives, cellular responses to external stimuli, and membrane. Module 2 consisted of 21 nodes and 41 edges (Fig. 4B). Hub genes in module 2 were significantly enriched in diseases of glycosylation and multicellular organismal process.

MiRNA-hub gene regulatory network construction

The miRNet database and Cytoscape software were used to establish the miRNA-hub gene regulatory network of the hub genes. A miRNA-hub gene regulatory network containing 2222 nodes (miRNAs: 1952 and hub genes: 270) and 9722 edges was constructed (Fig. 5). *tfr* that was modulated by 108 miRNAs (ex: hsa-mir-409-3p); *top2a* that was modulated by 90 miRNAs (ex: hsa-mir-320d); *cdk1* that was modulated by 68 miRNAs (ex hsa-mir-301a-5p); *cep55* that was modulated by 56 miRNAs (ex: hsa-mir-107); *fkbp5* that was modulated by 32 miRNAs (ex: hsa-mir-205-5p); *atn1* that was modulated by 74 miRNAs (ex: hsa-mir-3200-3p); *fscn1* that was modulated by 62 miRNAs (ex: hsa-mir-29a-5p); *cherp* that was modulated by 52 miRNAs (ex: hsa-mir-296-5p); *notch1* that was modulated by 35 miRNAs (ex: hsa-mir-139-5p); *notch3* that was modulated by 33 miRNAs (ex: hsa-mir-147a) (Table 5).

TF-hub gene regulatory network construction

The NetworkAnalyst database and Cytoscape software were used to establish the TF-hub gene regulatory network of the hub genes. A TF-hub gene regulatory network containing 356 nodes (TF: 78 and hub gene: 278) and 2152 edges was constructed (Fig. 6). *rps27* that was modulated by 18 TFs (ex; *creb1*); *fkbp5* that was

modulated by 17 TFs (ex; *tp63*); *tfr* that was modulated by 15 TFs (ex; *foxa1*); *cdk1* that was modulated by 14 TFs (ex; *nrf1*); *prdx1* that was modulated by 11 TFs (ex; *jund*); *atn1* that was modulated by 19 TFs (ex; *tead1*); *fscn1* that was modulated by 8 TFs (ex; *sreb2*); *atp6v1b1* that was modulated by 7 TFs (ex; *gata2*); *gata1* that was modulated by 7 TFs (ex; *e2f1*); *mrpl12* that was modulated by 7 TFs (ex; *tp53*) (Table 5).

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

To determine top hub genes have the diagnose significance of MI patients; The ROC analyses were conducted to explore the sensitivity and specificity of hub genes for MI diagnosis. The results showed that *cftr* (AUC=0.895), *cdk1* (AUC=0.915), *rps13* (AUC=0.962), *rps15a* (AUC=0.959), *rps27* (AUC=0.974), *notch1* (AUC=0.969), *mrpl12* (AUC=0.880), *nos2* (AUC=0.960), *ccdc85b* (AUC=0.933) and *atn1* (AUC=0.943) have the best diagnostic value for differentiating the patients with MI from normal controls (Fig. 7). This indicated that expression of hub genes include *cftr*; *cdk1*, *rps13*, *rps15a*, *rps27*, *notch1*, *mrpl12*, *nos2*, *ccdc85b* and *atn1* correlated with disease activity of MI, these hub genes could act as a biomarkers to estimate the activity of MI and verify the effectiveness of the treatment of MI.

Discussion

Disregarding of new development in the treatment of MI, it has continued the greater frequent cause of heart-related deaths in the past few years. The huge mortality rate of MI is slightly due to the inadequacy of acceptable screening methods with tremendous sensitivity and specificity. Therefore, it is essential to determine potential biomarkers for screening and early diagnosis of MI. NGS technology has become essential tools for providing complete genetic information on MI samples and prophetic the changes in disease advancement.

The present investigation obtained NGS dataset GSE132143 from the GEO database, and total of 958 DEGs were screened, including 480 up-regulated genes and 478 down-regulated genes were selected between

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

Pathway ID	Pathway Name	Adjusted p value	Negative log10 of adjusted p value	Gene Count	Gene
Up-regulated genes					
REAC:R-HSA-168256	Immune System	1.83563E-05	4.736214648	81	IL1RL1,SERPINA3,RNASE2,CD177,TUBA3C,PLA2G2A,S100A9,IL1R2,FPR1,CCL20,TUBA3D,DEFB1,S100A8,MCEMP1,S100A12,TUBA3E,TLR2,PTX3,CLEC4D,AREG,FCGR1A,FGF10,SIGLEC10,MUC16,CLEC4E,LILRA5,MGST1,CAMP,SLC11A1,LBP,IL18R1,RETN,CCR1,IGKV2D-40,TLR8,FCGR3A,SIGLEC12,F13A1,FCGR1B,CD53,MRC1,BIRC3,FPR2,CAA1,FCN3,GPR84,FLT3,TUBAL3,SIGLEC5,SIGLEC7,TREML4,FCER1G,SIGLEC9,CR1,TREM2,HP,IRAK3,LY96,BATF,CYBB,RHOU,CLEC7A,CTSC,C3AR1,IGHV3-48,RNASE6,CD180,MAOA,IGHV3-53,SLPI,APOB,FGF7,LCP1,HPSE,MAK3,KIF20A,TNFRSF11A,IL18RAP,CLEC12A,AP1S2,C7
REAC:R-HSA-168249	Innate Immune System	1.83563E-05	4.736214648	51	SERPINA3,RNASE2,CD177,PLA2G2A,S100A9,FPR1,DEFB1,S100A8,MCEMP1,S100A12,TLR2,PTX3,CLEC4D,FCGR1A,MUC16,CLEC4E,MGST1,CAMP,SLC11A1,LBP,RETN,IGKV2D-40,TLR8,FCGR3A,CD53,BIRC3,FPR2,CAA1,FCN3,GPR84,SIGLEC5,FCER1G,SIGLEC9,CR1,TREM2,HP,IRAK3,LY96,CYBB,CLEC7A,CTSC,C3AR1,IGHV3-48,RNASE6,CD180,IGHV3-53,SLPI,APOB,HPSE,CLEC12A,C7
REAC:R-HSA-6798695	Neutrophil degranulation	9.54101E-05	4.020405579	29	SERPINA3,RNASE2,CD177,S100A9,FPR1,S100A8,MCEMP1,S100A12,TLR2,PTX3,CLEC4D,MGST1,CAMP,SLC11A1,RETN,CD53,FPR2,GPR84,SIGLEC5,FCER1G,SIGLEC9,CR1,HP,CYBB,CTSC,C3AR1,SLPI,HPSE,CLEC12A
REAC:R-HSA-168898	Toll-like Receptor Cascades	0.012127308	1.916235606	12	S100A9,S100A8,S100A12,TLR2,LBP,TLR8,BIRC3,CAA1,IRAK3,LY96,CD180,APOB
REAC:R-HSA-71291	Metabolism of amino acids and derivatives	0.024436592	1.611959361	18	GLUL,BCAT1,KMO,NQO1,AASS,RPL39,RIDA,GNMT,CTH,RPL22L1,AMD1,RPS29,RPL26,RPS15A,SAT1,RPS13,EEF1E1,RPS27
REAC:R-HSA-8953897	Cellular responses to external stimuli	0.024436592	1.611959361	24	TUBA3C,TUBA3D,MT1A,TUBA3E,MT1X,H1-3,H2BC14,TUBAL3,H2BC9,H2BC3,CYBB,RPL39,H2AC14,H2BC11,H1-5,RPL22L1,FKBP5,RPS29,HIGD1A,RPL26,RPS15A,PRDX1,RPS13,RPS27
Down-regulated genes					
REAC:R-HSA-112316	Neuronal System	0.000114227	3.942232869	24	SYT12,LRFN1,NGG8,NRGN,CACNG8,ACHE,NRXN2,SHANK1,KCNN1,KCNJ9,PANX2,KCNF1,KCNC3,BEGAIN,GRIK4,SLC17A7,SHANK2,IL1RAPL2,GNB3,SLC6A1,SLC1A7,CPLX1,KCNK7,DLGAP4
REAC:R-HSA-1474244	Extracellular matrix organization	0.000114227	3.942232869	20	CAPN6,FBN3,CTRB2,COL22A1,ADAMTS14,COL1A1,CTRB1,TMPRSS6,COL20A1,BGN,AGRIN,COL9A1,COL11A2,LTBP4,LTBP2,COMP,LTBP3,LOXL2,COL5A1,COL9A2
REAC:R-HSA-6794362	Protein–protein interactions at synapses	0.012465304	1.904297133	8	SYT12,LRFN1,NRXN2,SHANK1,BEGAIN,SHANK2,IL1RAPL2,DLGAP4
REAC:R-HSA-1474228	Degradation of the extracellular matrix	0.015320837	1.814717503	10	CAPN6,FBN3,CTRB2,COL1A1,CTRB1,TMPRSS6,COL9A1,COL11A2,COL5A1,COL9A2
REAC:R-HSA-500792	GPCR ligand binding	0.030591053	1.514405578	19	PENK,APLN,R,CC13L1,NGG8,GLP1R,UTS2R,PLPPR3,ADRA2A,OXER1,DRD1,CCL3,ADRA1D,SCT,GNB3,RXFP4,OXT,S1PR5,ADGRE3,WNT10B
REAC:R-HSA-3781865	Diseases of glycosylation	0.093732211	1.028111137	8	MUC12,MUC3A,MUC5B,ADAMTS14,BGN,AGRIN,NOTCH3,NOTCH1

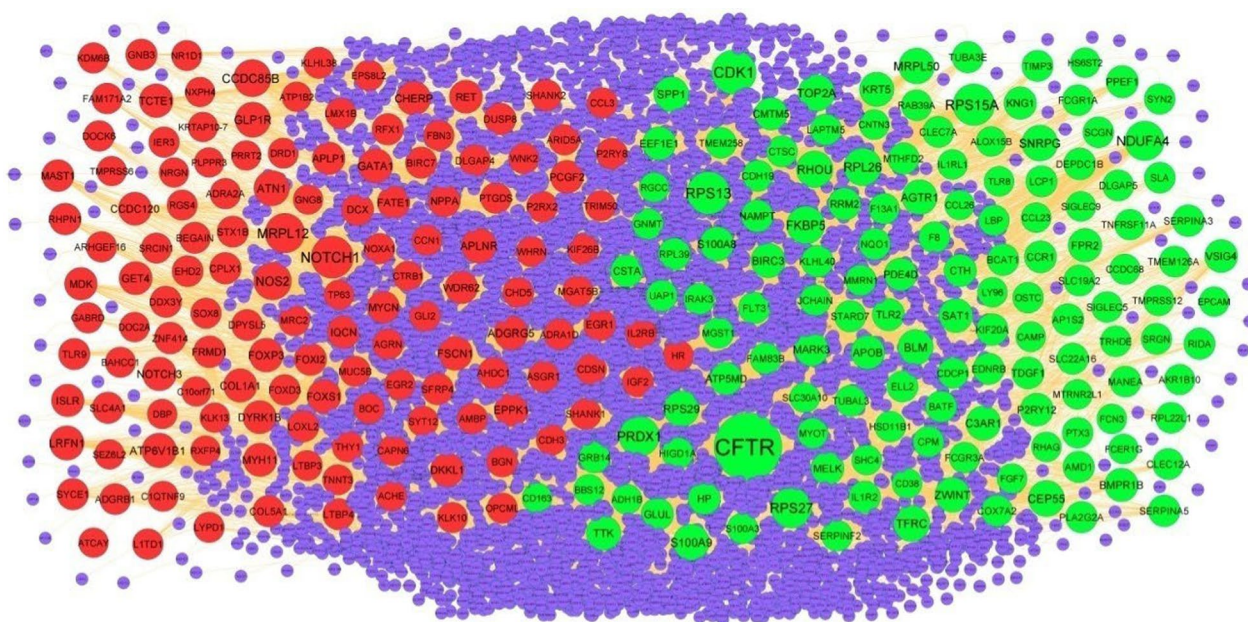


Fig. 3 PPI network of DEGs. Up-regulated genes are marked in green; down-regulated genes are marked in red

the MI samples and normal control samples. Research have shown that genes include *il1r1l* [40] and *alox15b* [41] plays an important role in the pathogenesis of coronary artery disease. Some studies have shown that altered expression of genes include *serpina3* [42], *gpr78* [43] and *esm1* [44] promotes the MI. A study indicates that *scgn* has been identified in diabetes mellitus [45]. These genes served as potential biomarkers for MI diagnosis and prognosis.

In this investigation, we identified enriched genes in GO terms and signaling pathways that might be utilized as diagnostic and/or therapeutic targets in MI. GO terms and signaling pathways include immune system [46], innate immune system [47], neutrophil degranulation [48], toll-like receptor cascades [49], metabolism of amino acids and derivatives [50], neuronal system [51], extracellular matrix organization [52], degradation of the extracellular matrix [53], diseases of glycosylation [54], response to stimulus [55], cell communication [56], cell periphery [57], membrane [58], anatomical structure development [59] and plasma membrane [60] were responsible for progression of MI. Recently, mounting researches have revealed that genes include *pla2g2a* [61], *ccl23* [62], *cd53* [63], *trem14* [64], *trem2* [65], *cd180* [66], *hpse* [67], *cela2a* [68], *tnfrsf4* [69], *ambp* [70], *sox18* [71], *panx2* [72], *rspo2* [73], *comp* [74], *asgr1* [75] and *noxa1* [76] were vital for the onset and developmental process of atherosclerosis. A great number of studies have indicated that genes include *s100a9* [77], *adora3* [78], *il1r2* [79], *fpr1* [80], *ccl20* [81], *cd163* [82], *s100a8* [83], *tlr2*

[84], *has2* [85], *ptx3* [86], *timp4* [87], *areg* [88], *lbp* [89], *il18r1* [90], *alox5ap* [91], *retn* [92], *f13a1* [93], *fpr2* [94], *saa1* [95], *flt3* [96], *aqp4* [97], *fcer1g* [98], *ccl18* [99], *hp* [100], *cdk1* [101], *slc7a11* [102], *cftr* [103], *f8* [104], *stc1* [44], *il18rap* [90], *timp3* [105], *pde4d* [106], *cyp4a11* [107], *scn10a* [108], *apob* [109], *ace* [110], *penk* [111], *hspb6* [112], *tlr9* [113], *egr1* [114], *cacng8* [115], *foxd3* [116], *dbh* [117], *foxp3* [118], *glp1r* [119], *il34* [120], *ccn1* [121], *adra2a* [122], *bgn* [123], *nos2* [124], *agnr* [125], *drd1* [126], *gnb3* [127], *egr2* [128], *mdk* [129], *notch3* [130], *azin2* [131], *notch1* [132], *lox12* [133], *adamts14* [134] and *sod3* [135] have been implicated in MI pathology.. A previous bioinformatics study suggested that genes include *defb1* [136], *slc11a1* [137], *spink1* [138], *ccr1* [139], *glul* [140], *gpr84* [141], *siglec5* [142], *siglec7* [143], *lgr5* [144], *cd38* [145], *grb14* [146], *prdx1* [147], *slc19a2* [148], *cadm2* [149], *trpm5* [150], *col1a1* [151], *ctrb1* [152], *uts2r* [153], *crtc1* [154], *muc5b* [155], *tmprss6* [156], *slc5a2* [157] and *kcj9* [158] might play a role in the development of diabetes mellitus. A previous study reported that the genes include *mt1a* [159], *lyve1* [160], *s100a12* [161], *gckr* [162], *tlr8* [163], *mrc1* [164], *agtr1* [165], *p2ry12* [166], *msr1* [167], *nqo1* [168], *fkbp5* [169], *cmtm5* [170], *adh1c* [171], *aplnr* [172], *sfrp4* [173], *ccl3* [174], *col11a2* [175], *egr3* [176] and *il2rb* [177] play an important role in the pathophysiology of coronary artery disease. Study demonstrated that genes include *edn2* [178], *snx10* [179] and *kcnn1* [180] can participate in the occurrence and development of atrial fibrillation. The abnormal expression of genes include *ednrb* [181],

Table 4 Topology table for up- and down-regulated genes

Regulation	Node	Degree	Betweenness	Stress	Closeness
Up	CFTR	800	0.250818	2.82E+08	0.382037
Up	CDK1	289	0.059973	1.09E+08	0.333174
Up	RPS13	255	0.037331	50,801,568	0.35159
Up	RPS15A	233	0.031358	47,775,876	0.332312
Up	RPS27	213	0.025226	52,139,390	0.332277
Up	PRDX1	201	0.034128	55,983,910	0.348223
Up	NDUFA4	190	0.041688	59,296,328	0.316656
Up	FKBP5	157	0.031733	44,198,116	0.315591
Up	RPL26	156	0.014756	28,200,346	0.320904
Up	RHOU	133	0.032899	14,114,804	0.299016
Up	TOP2A	132	0.022582	21,447,746	0.337518
Up	TFRC	127	0.026876	31,508,150	0.324479
Up	S100A9	124	0.023694	18,575,534	0.334877
Up	CEP55	123	0.022005	29,250,578	0.306355
Up	SNRPG	121	0.022174	58,988,410	0.287667
Up	MRPL50	117	0.017338	16,197,166	0.294992
Up	RPS29	111	0.007838	10,474,252	0.313312
Up	BLM	108	0.021289	16,918,168	0.325049
Up	AGTR1	100	0.022019	17,157,708	0.305566
Up	ZWINT	99	0.018375	20,533,060	0.291506
Up	SPP1	99	0.018586	9,330,572	0.314503
Up	C3AR1	94	0.016166	25,287,748	0.264361
Up	TTK	91	0.017179	19,765,014	0.304974
Up	BIRC3	90	0.014977	24,960,018	0.299957
Up	KRT5	90	0.008929	25,389,258	0.305804
Up	S100A8	88	0.012007	12,637,402	0.333298
Up	SAT1	82	0.014165	15,900,742	0.297742
Up	APOB	78	0.01467	14,861,278	0.302962
Up	MARK3	76	0.010936	15,499,698	0.29433
Up	FPR2	74	0.011396	18,351,388	0.256034
Up	BMPRI1B	71	0.013222	16,342,524	0.29051
Up	EEF1E1	67	0.006446	9,571,868	0.295922
Up	VSIG4	64	0.011875	13,237,432	0.278326
Up	MELK	63	0.009324	6,151,010	0.281124
Up	P2RY12	63	0.008425	7,797,394	0.272302
Up	PDE4D	54	0.007393	10,017,988	0.303913
Up	CMTM5	54	0.011555	15,349,250	0.261776
Up	CTH	54	0.011322	13,403,074	0.277137
Up	KNG1	53	0.008809	6,029,112	0.28506
Up	GLUL	51	0.007775	12,036,292	0.288989
Up	HP	51	0.005073	7,718,948	0.292292
Up	RRM2	50	0.006974	4,018,526	0.318226
Up	TLR2	50	0.009032	7,171,472	0.28207
Up	PPEF1	49	0.002383	6,116,412	0.275197
Up	ATP5MD	49	0.005997	5,678,794	0.29341
Up	NAMPT	48	0.005236	8,796,778	0.285864
Up	CSTA	47	0.0056	3,242,708	0.312876
Up	CCR1	46	0.008862	10,277,030	0.260572
Up	TDGF1	45	0.006828	11,958,282	0.265074

Table 4 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness
Up	RPL39	43	0.003737	9,890,538	0.279749
Up	KIF20A	42	0.0056	10,002,414	0.277112
Up	IL1R2	42	0.007887	2,661,112	0.297096
Up	SERPINA3	42	0.007121	5,931,062	0.279762
Up	DEPDC1B	42	0.003267	3,787,682	0.261395
Up	KLHL40	42	0.006323	6,412,684	0.260551
Up	SERPINA5	41	0.005996	5,510,082	0.271082
Up	AP1S2	39	0.006525	11,289,512	0.276333
Up	BCAT1	38	0.007672	4,563,422	0.267509
Up	FLT3	37	0.004	5,164,642	0.274106
Up	PLA2G2A	35	0.004359	5,431,086	0.276091
Up	NQO1	34	0.002866	9,438,888	0.275329
Up	COX7A2	34	0.003955	2,248,426	0.279252
Up	MTHFD2	34	0.004247	7,481,058	0.27486
Up	TUBA3E	34	0.003142	6,571,258	0.277846
Up	HIGD1A	33	0.003446	5,562,624	0.282146
Up	AMD1	32	0.008064	2,564,908	0.281351
Up	EDNRB	31	0.004132	10,397,624	0.254141
Up	STARD7	31	0.004386	8,133,746	0.262958
Up	TIMP3	30	0.005329	5,535,204	0.271761
Up	SLC19A2	30	0.007143	2,466,610	0.27182
Up	SLC22A16	30	0.003748	5,590,640	0.231168
Up	BATF	29	0.005488	8,241,746	0.246551
Up	LAPTM5	29	0.002531	5,891,300	0.255805
Up	LCP1	29	0.003421	10,760,010	0.256367
Up	DLGAP5	28	0.003726	3,577,874	0.310085
Up	RIDA	28	0.003761	2,634,098	0.263586
Up	F8	27	0.003666	5,060,182	0.265499
Up	FCGR1A	27	0.003253	3,749,296	0.248646
Up	CLEC12A	27	0.004847	4,563,254	0.248371
Up	TUBAL3	27	0.001767	5,494,636	0.269076
Up	TMEM126A	27	0.004645	1,707,450	0.287773
Up	ELL2	26	0.003436	3,333,898	0.250877
Up	CDH19	26	0.004185	1,563,734	0.272008
Up	UAP1	25	0.002146	2,800,316	0.274177
Up	IRAK3	25	0.002929	4,503,640	0.259916
Up	CTSC	25	0.002683	4,792,556	0.257143
Up	MANEA	25	0.004902	1,598,406	0.248244
Up	CLEC7A	25	0.005317	2,453,022	0.27107
Up	GRB14	24	0.003207	4,733,128	0.272137
Up	GNMT	24	0.001794	2,840,784	0.262881
Up	FAM83B	24	0.002446	4,019,758	0.270802
Up	RPL22L1	24	0.004024	2,944,142	0.283123
Up	JCHAIN	24	0.004353	4,653,652	0.252134
Up	SIGLECS	24	0.003229	1,035,168	0.250897
Up	SLA	23	0.002594	3,046,528	0.271714
Up	CPM	23	0.002164	3,067,630	0.259937
Up	SCGN	22	0.003827	7,053,140	0.244529
Up	SERPINF2	21	0.001762	2,060,048	0.253639

Table 4 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness
Up	RAB39A	21	0.002987	3,242,160	0.275848
Up	FCGR3A	20	0.003232	3,079,286	0.261689
Up	TNFRSF11A	19	0.001994	2,676,430	0.259798
Up	PTX3	19	0.004185	3,863,002	0.223943
Up	SRGN	19	0.001867	1,548,928	0.257754
Up	LBP	19	0.001897	2,861,646	0.255503
Up	SYN2	19	0.001206	3,610,072	0.24756
Up	MMRN1	19	0.001393	927,204	0.252144
Up	OSTC	19	0.002529	2,572,846	0.272574
Up	TMEM258	19	0.002276	3,475,832	0.257691
Up	F13A1	18	0.001232	1,483,048	0.25413
Up	HSD11B1	18	0.003099	2,861,348	0.256347
Up	S100A3	17	0.00276	4,485,872	0.243989
Up	MYOT	17	0.001723	1,802,236	0.260411
Up	BBS12	17	0.00243	8,403,578	0.23358
Up	TRHDE	17	0.00403	3,288,960	0.265847
Up	TMPRSS12	17	0.002815	3,369,698	0.239721
Up	CDCP1	16	0.003614	2,357,734	0.278387
Up	SLPI	15	9.63E-04	976,730	0.259733
Up	AKR1B10	15	0.001132	493,918	0.266952
Up	MGST1	14	9.56E-04	1,544,300	0.273665
Up	CCDC68	14	0.001456	2,365,346	0.237504
Up	SIGLEC9	2	8.70E-06	23,072	0.225419
Up	ADH1B	2	4.07E-05	37,458	0.22735
Up	TLR8	2	0	0	0.213827
Up	CAMP	2	7.42E-05	96,406	0.218962
Up	CCL23	1	0	0	0.206716
Up	RGCC	1	0	0	0.249921
Up	CD38	1	0	0	0.207418
Up	EPCAM	1	0	0	0.276442
Up	LY96	1	0	0	0.220019
Up	HS6ST2	1	0	0	0.216991
Up	SHC4	1	0	0	0.219581
Up	ALOX15B	1	0	0	0.214096
Up	FCN3	1	0	0	0.182974
Up	MTRNR2L1	1	0	0	0.258294
Up	IL1RL1	1	0	0	0.213269
Up	FGF7	1	0	0	0.229943
Up	CNTN3	1	0	0	0.228714
Up	CCL26	1	0	0	0.206716
Up	CD163	1	0	0	0.226189
Up	SLC30A10	1	0	0	0.244996
Up	FCER1G	1	0	0	0.207418
Up	RHAG	1	0	0	0.208291
Down	NOTCH1	250	0.055026	75,882,802	0.332417
Down	MRPL12	195	0.037118	50,798,784	0.313578
Down	NOS2	158	0.017276	30,450,186	0.318499
Down	CCDC85B	151	0.033004	20,747,204	0.302234
Down	ATN1	114	0.02349	18,276,352	0.303108

Table 4 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness
Down	GLP1R	109	0.025463	18,684,482	0.290591
Down	APLNR	103	0.021689	18,858,734	0.291736
Down	ATP6V1B1	99	0.022959	9,935,628	0.299714
Down	LRFN1	93	0.015879	12,549,670	0.28071
Down	GATA1	89	0.015617	23,510,800	0.300372
Down	FSCN1	88	0.013048	8,110,734	0.32723
Down	CHERP	84	0.011161	20,724,310	0.296983
Down	EPPK1	84	0.012839	12,039,586	0.333016
Down	FOXP3	83	0.011715	20,499,710	0.28292
Down	NOTCH3	80	0.015072	8,290,510	0.312643
Down	ADGRG5	80	0.015847	20,888,478	0.264461
Down	TCTE1	80	0.015977	7,802,718	0.285838
Down	FOXS1	79	0.012498	20,736,510	0.282526
Down	DKKL1	78	0.016678	18,615,684	0.276503
Down	COL1A1	76	0.013725	12,697,230	0.29859
Down	MYH11	73	0.009346	5,311,188	0.31947
Down	DYRK1B	71	0.011062	18,710,680	0.285747
Down	GET4	68	0.010111	18,051,758	0.298392
Down	CCDC120	68	0.017344	9,691,046	0.297898
Down	RET	67	0.010929	10,583,060	0.304811
Down	PCGF2	64	0.010749	21,781,650	0.281439
Down	APLP1	61	0.014188	6,846,322	0.296521
Down	MDK	59	0.009935	11,348,532	0.286815
Down	WDR62	58	0.008676	12,733,168	0.289908
Down	ISLR	58	0.010523	20,009,526	0.260238
Down	IQC�	57	0.010111	16,769,670	0.269053
Down	FATE1	57	0.011652	14,232,246	0.251328
Down	FOXI2	53	0.007592	8,828,670	0.261211
Down	DCX	48	0.009089	5,176,554	0.304163
Down	EGR1	47	0.006697	16,123,798	0.27545
Down	MAST1	47	0.007072	12,364,366	0.29121
Down	MYCN	46	0.0041	6,582,592	0.280085
Down	NPPA	46	0.009645	4,323,078	0.272408
Down	FRMD1	45	0.009925	7,849,260	0.246165
Down	COL5A1	40	0.005986	5,359,170	0.28479
Down	DUSP8	40	0.005631	2,465,084	0.282869
Down	RHPN1	40	0.006169	4,790,624	0.257553
Down	SFRP4	40	0.005898	8,543,724	0.267816
Down	CPLX1	39	0.007959	3,871,650	0.275028
Down	ZNF414	39	0.006946	10,943,040	0.246175
Down	RFX1	38	0.007136	2,569,940	0.29763
Down	LOXL2	38	0.005758	9,246,234	0.275077
Down	SLC4A1	37	0.005974	7,496,290	0.263079
Down	SYCE1	37	0.005509	11,144,044	0.255753
Down	DDX3Y	37	0.002711	5,323,020	0.281363
Down	SHANK2	36	0.005424	4,374,242	0.3001
Down	LTBP4	36	0.005445	2,434,208	0.266839
Down	BIRC7	35	0.003199	5,467,760	0.251148
Down	GNB3	35	0.00595	9,751,722	0.264328

Table 4 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness
Down	BEGAIN	33	0.003947	3,860,650	0.270814
Down	TLR9	33	0.004504	7,136,794	0.260045
Down	DLGAP4	33	0.00457	5,414,044	0.281388
Down	SHANK1	32	0.003386	4,979,252	0.259476
Down	STX1B	32	0.004463	9,748,988	0.239712
Down	THY1	32	0.003414	4,184,066	0.262049
Down	KLHL38	32	0.004726	5,878,076	0.26425
Down	IL2RB	31	0.004268	8,195,548	0.269745
Down	EHD2	30	0.003516	11,343,860	0.241776
Down	P2RY8	29	0.003672	4,881,448	0.246967
Down	DPYSL5	28	0.003752	5,602,212	0.264183
Down	MRC2	28	0.00602	3,155,886	0.285009
Down	ADGRB1	27	0.003534	4,457,434	0.253628
Down	CHD5	27	0.002936	5,717,864	0.271035
Down	P2RX2	26	0.004522	6,083,842	0.242437
Down	PTGDS	25	0.003159	4,128,644	0.268204
Down	IGF2	24	0.002926	3,579,840	0.254367
Down	AHDC1	24	0.002394	2,714,014	0.284854
Down	FAM171A2	24	0.003962	4,336,600	0.250468
Down	MGAT5B	23	0.003457	1,490,980	0.239338
Down	KIF26B	23	0.003064	1,399,770	0.286384
Down	DOCK6	23	0.00371	4,300,742	0.254511
Down	ASGR1	23	0.003218	3,830,722	0.282424
Down	FOXD3	23	0.00188	986,110	0.270464
Down	BGN	22	0.004658	1,408,836	0.280173
Down	CDSN	22	0.002468	1,014,552	0.281514
Down	AGRN	22	0.003369	1,782,196	0.290981
Down	ARID5A	22	0.002375	2,661,748	0.264206
Down	L1TD1	22	0.003525	5,054,094	0.240491
Down	LMX1B	21	0.002896	2,846,334	0.268789
Down	EGR2	21	0.002473	1,703,458	0.254934
Down	GLI2	20	0.002149	2,685,102	0.281477
Down	ADRA2A	20	0.001974	3,308,074	0.251751
Down	ARHGEF16	20	0.00193	4,148,570	0.270872
Down	WNK2	20	0.001619	3,205,596	0.269745
Down	ADRA1D	19	0.001854	3,465,836	0.250139
Down	GABRD	19	0.002153	2,302,972	0.235169
Down	CAPN6	19	0.002692	4,506,702	0.244093
Down	LYPD1	19	0.002765	4,063,698	0.241118
Down	SOX8	19	0.003288	2,741,798	0.250787
Down	IER3	18	0.004052	2,238,378	0.283851
Down	NOXA1	18	0.002917	2,744,574	0.267611
Down	EPS8L2	18	0.001633	1,924,974	0.278289
Down	KDM6B	18	0.002083	2,000,150	0.252823
Down	AMBP	17	8.61E-04	1,420,600	0.275873
Down	BOC	17	0.002632	3,509,404	0.255742
Down	KLK10	17	0.001916	2,746,686	0.246484
Down	BAHCC1	16	0.002208	3,217,268	0.259081
Down	WHRN	16	0.002154	2,204,088	0.243168

Table 4 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness
Down	MUC5B	16	0.003777	2,428,884	0.25688
Down	OPCML	16	0.001443	1,865,180	0.251409
Down	SYT12	16	0.002859	4,959,848	0.230735
Down	RGS4	15	0.002083	3,512,584	0.257101
Down	NR1D1	15	0.002637	2,458,946	0.259177
Down	HR	15	0.001354	2,193,650	0.262738
Down	ACHE	15	0.002614	1,339,788	0.27682
Down	CDH3	15	0.001266	415,460	0.294178
Down	SRCIN1	15	0.001085	1,237,478	0.267919
Down	TRIM50	15	0.001172	1,853,618	0.236255
Down	C1QTNF9	15	0.001478	1,276,520	0.225274
Down	LTBP3	15	0.001739	1,944,214	0.243837
Down	FBN3	15	0.001381	2,246,422	0.25167
Down	CCL3	14	0.001829	714,350	0.242465
Down	DRD1	14	0.002047	3,743,596	0.239639
Down	CCN1	14	0.001042	583,294	0.268605
Down	TNNT3	14	0.00141	1,015,768	0.216983
Down	KRTAP10-7	3	1.01E-04	108,030	0.237012
Down	TP63	2	1.10E-05	54,194	0.241859
Down	CTRB1	2	1.23E-05	15,314	0.225881
Down	KLK13	2	1.23E-05	15,314	0.225881
Down	GNG8	1	0	0	0.209073
Down	DOC2A	1	0	0	0.196489
Down	DBP	1	0	0	0.197793
Down	NRGN	1	0	0	0.225169
Down	ATCAY	1	0	0	0.200856
Down	PLPPR3	1	0	0	0.209156
Down	C10orf71	1	0	0	0.22225
Down	SEZ6L2	1	0	0	0.229055
Down	TMPRSS6	1	0	0	0.229943
Down	NXPH4	1	0	0	0.230195
Down	PRRT2	1	0	0	0.211122
Down	RXFP4	1	0	0	0.221834
Down	ATP1B2	1	0	0	0.242952

fgf10 [182], *wnk3* [183], *kng1* [184], *fcn3* [185], *aqp3* [186], *hpr* [187], *cth* [188], *sparcl1* [189], *maoa* [190], *bmpr1b* [191], *fgf7* [192], *calcl1* [193], *mark3* [194], *adh1b* [195], *amh* [196], *ret* [197], *igf2* [198], *slc6a9* [199], *nppa* [200], *sct* [201], *dcx* [202], *asic1* [203], *lmx1b* [204], *dbp* [205] and *slc6a9* [206] contributes to the progression of hypertension. Study showed that the genes include *camp* [207], *spp1* [208], *cxcl11* [209], *tfr3* [210], *irak3* [211], *c3ar1* [212], *gli2* [213], *thy1* [214], *foxo6* [215], *rgs4* [216], *wnt10b* [217] and *aebp1* [218] plays a vital role in the development of might be related to the pathophysiology of obesity. A study showed genes include *tdgf1* [219], *kif20a* [220] and *ltbp2* [221] are highly prone to

congenital heart defect. Our data indicated that enriched genes might have impact on MI progression. It would be meaningful to confirm exact function of enriched genes in MI in prospective.

Building PPI network is favorable for investigators to study the underlying molecular mechanism of MI for the reason that the DEGs would be unified and organized in the network deciding by their interactions. Identification of hub genes that might be key prognostic markers, diagnostic markers and therapeutic targets for MI. Based on the PPI network constructed by the online database HIPIE, we identified hub genes. A recent study suggested that the hub genes include *cfr* [103], *cdk1* [101], *notch1*

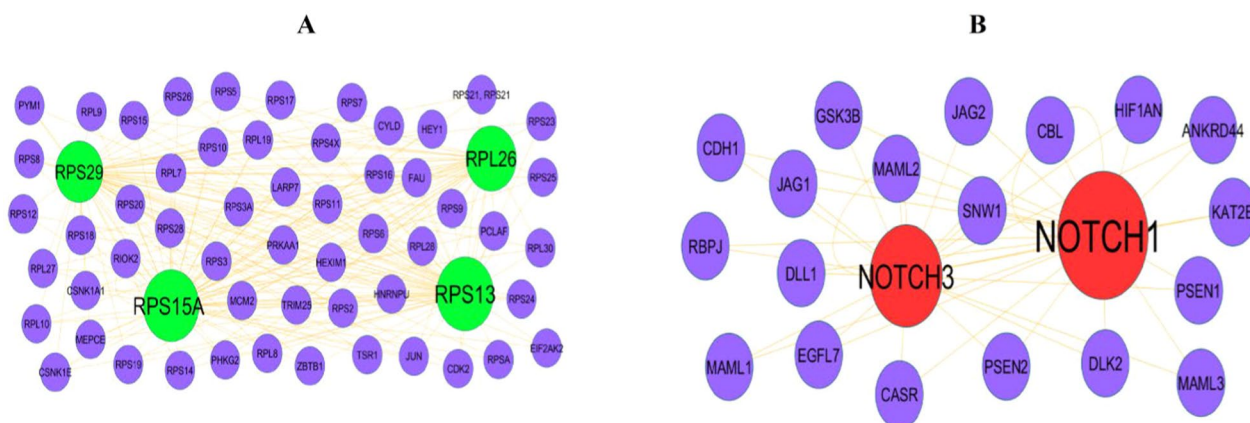


Fig. 4 Modules of isolated form PPI of DEGs. (A) The most significant module was obtained from PPI network with 59 nodes and 203 edges for up-regulated genes (B). The most significant module was obtained from PPI network with 21 nodes and 41 edges for down-regulated genes. Up-regulated genes are marked in green; down-regulated genes are marked in red

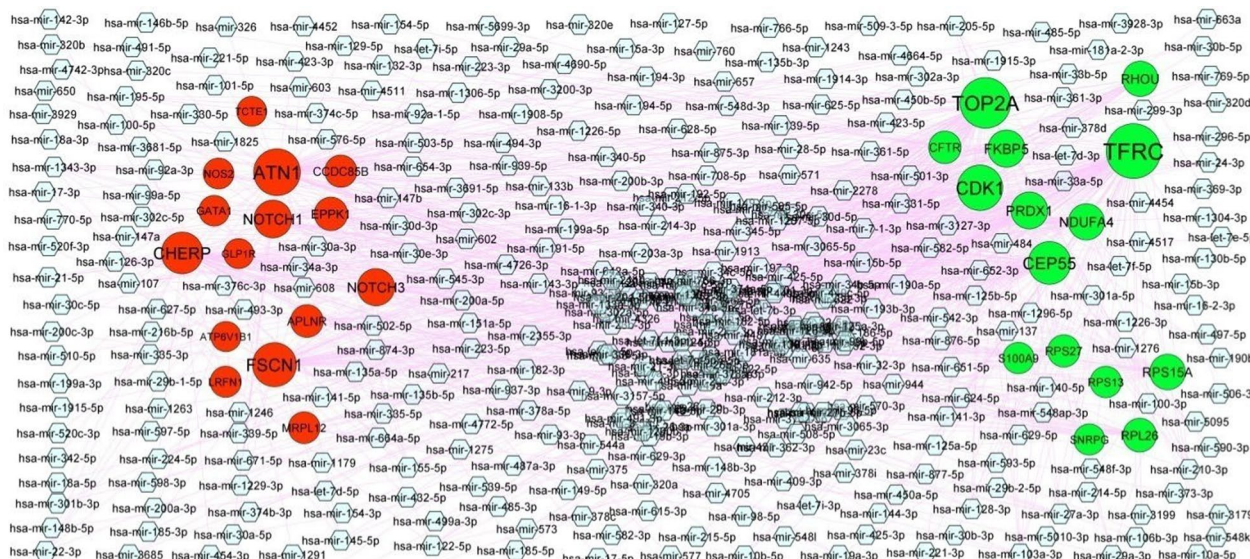


Fig. 5 Target gene—miRNA regulatory network between target genes. The blue color diamond nodes represent the key miRNAs; up-regulated genes are marked in green; down-regulated genes are marked in red

[132], *nos2* [124] and *notch3* [130] might take part in the progression of MI. We gave a new confirmation for that *rps13*, *rps15a*, *rps27*, *rpl26*, *rps29*, *mrpl12*, *ccdc85b* and *atn1* are expected to become a novel biomarker for MI prognosis. Thus, it might consider as potential therapeutic targets for MI.

To illuminate the potential molecular mechanism of the hub genes in MI, we focused a miRNA-hub gene regulatory network and TF-hub gene regulatory network analysis. The identified hub genes, TFs and miRNAs might be associated in the pathological process of MI. Zaja et al. [101], Si et al. [132], Zhang et al. [130],

Chen et al. [222], Li and Zhang [223], Wang et al. [224], Zhao et al. [225], Lin et al. [226], Liao et al. [227], Izadpanah et al. [228], Wang et al. [229] and Hakobjanyan et al. [230] reported that the expression of the *cdk1*, *notch1*, *notch3*, *hsa-mir-409-3p*, *hsa-mir-320d*, *hsa-mir-107*, *hsa-mir-139-5p*, *nrf1*, *tead1*, *gata2*, *e2f1* and *tp53* can lead to MI. Studies reported that biomarkers include *hsa-mir-301a-5p* [231], *hsa-mir-29a-5p* [232], *hsa-mir-296-5p* [233], *creb1* [234] and *foxa1* [235] were proposed to contribute to the development of diabetes mellitus. A previous study reported that *hsa-mir-205-5p* plays a key role in hypertension [236].

Table 5 miRNA—target gene and TF—target gene interaction

Regulation	Target Genes	Degree	MicroRNA	Regulation	Target Genes	Degree	TF
Up	TFRC	108	hsa-mir-409-3p	Up	RPS27	18	CREB1
Up	TOP2A	90	hsa-mir-320d	Up	FKBP5	17	TP63
Up	CDK1	68	hsa-mir-301a-5p	Up	TFRC	15	FOXA1
Up	CEP55	56	hsa-mir-107	Up	CDK1	14	NRF1
Up	FKBP5	32	hsa-mir-205-5p	Up	PRDX1	11	JUND
Up	PRDX1	31	hsa-mir-18a-3p	Up	CFTR	10	RUNX2
Up	NDUFA4	28	hsa-mir-185-5p	Up	RHOU	10	SOX17
Up	RPS15A	25	hsa-mir-571	Up	RPS13	10	FOXF2
Up	RHOU	24	hsa-mir-340-5p	Up	RPS15A	9	FOXC1
Up	RPL26	17	hsa-mir-200a-5p	Up	TOP2A	8	SRF
Up	CFTR	12	hsa-mir-4452	Up	CEP55	7	NFIC
Up	RPS27	11	hsa-mir-103a-3p	Up	RPL26	7	ZNF354C
Up	RPS13	7	hsa-mir-126-3p	Up	SNRPG	5	ELK4
Up	S100A9	7	hsa-mir-1343-3p	Up	NDUFA4	3	RELA
Up	SNRPG	6	hsa-mir-155-5p	Up	S100A9	2	USF2
Down	ATN1	74	hsa-mir-3200-3p	Down	ATN1	19	TEAD1
Down	FSCN1	62	hsa-mir-29a-5p	Down	FSCN1	8	SREBF2
Down	CHERP	52	hsa-mir-296-5p	Down	ATP6V1B1	7	GATA2
Down	NOTCH1	35	hsa-mir-139-5p	Down	GATA1	7	E2F1
Down	NOTCH3	33	hsa-mir-147a	Down	MRPL12	7	TP53
Down	EPPK1	16	hsa-mir-148b-3p	Down	CHERP	7	PPARG
Down	APLNR	13	hsa-mir-373-3p	Down	GLP1R	6	ARID3A
Down	CCDC85B	11	hsa-mir-603	Down	FOXP3	6	STAT3
Down	MRPL12	9	hsa-mir-128-3p	Down	NOTCH3	6	KLF5
Down	LRFN1	6	hsa-mir-145-5p	Down	EPPK1	5	E2F6
Down	NOS2	5	hsa-mir-497-5p	Down	APLNR	4	PRDM1
Down	GATA1	4	hsa-mir-4454	Down	NOS2	4	IRF2
Down	ATP6V1B1	2	hsa-mir-1229-3p	Down	NOTCH1	3	GATA3
Down	GLP1R	1	hsa-mir-376c-3p	Down	LRFN1	3	YY1
Down	TCTE1	1	hsa-mir-7-5p	Down	CCDC85B	3	TFAP2A

Accumulated evidence has demonstrated that biomarkers include *fkbp5* [169] and *sreb2* [237] are associated with coronary artery disease. Studies have shown that biomarker *tfrc* (transferrin receptor) [210] was identified to be associated with obesity. Our interesting finding is that novel biomarkers include *top2a*, *cep55*, *fscn1*, *cherp*, *atp6v1b1*, *gata1*, *hsa-mir-3200-3p*, *hsa-mir-147a*, *tp63* and *jund* (jun D proto-oncogene) are all closely related to MI. Evidence from studies indicates that these novel biomarkers might be related to the advancement of MI and thus has the potential to be used as a diagnostic biomarkers of MI.

Our investigations had some limitations. Firstly, we used only 1 dataset, and there might have been bias in the search for biomarkers for MI. Secondly, we did not account for the potential confounding effects of demographic variables. Finally, we did not carry out experiments to prove the research results, which will

be considered in future work. Finally, we did not carry out in vivo and in vitro validation experiments for hub genes to prove the research results, which will be considered in future work.

Conclusion

This investigation identified significant DEGs between MI and normal control samples via analyzing NGS dataset. *cftr*, *cdk1*, *rps13*, *rps15a*, *rps27*, *notch1*, *mrpl12*, *nos2*, *ccdc85b* and *atn1* were verified and considered as hub genes were linked with disease prognosis, which could be predictive and therapeutic targets. The above results provide novel investigation directions for the relationship between MI and its associated complications. Bioinformatics and NGS technology provide opportunities to further examine the molecular mechanism and targeted therapy of MI on a transcriptional

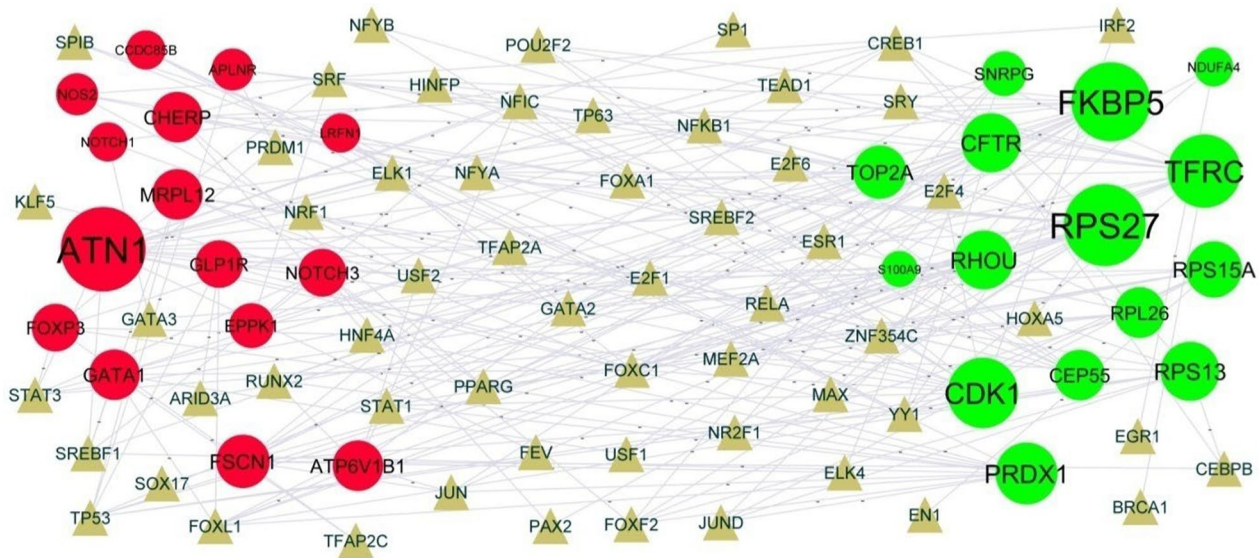


Fig. 6 Target gene—TF regulatory network between target genes. The gray color triangle nodes represent the key TFs; up-regulated genes are marked in green; down-regulated genes are marked in red

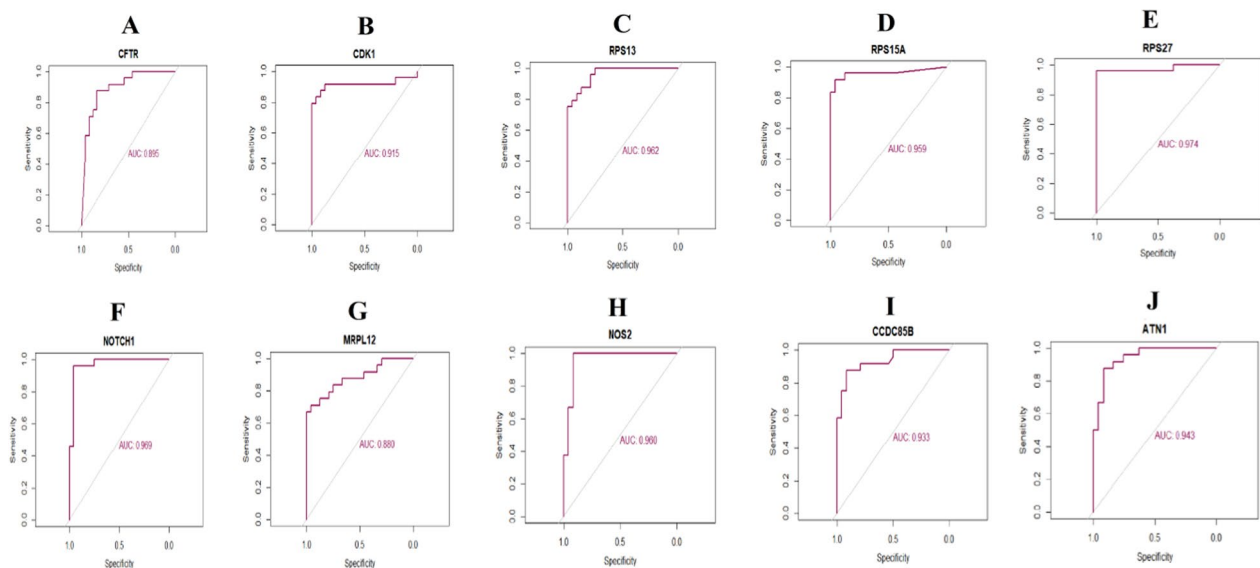


Fig. 7 ROC curve analyses of hub genes. **A** CFTR, **B** CDK1, **C** RPS13, **D** RPS15A, **E** RPS27, **F** NOTCH1, **G** MRPL12, **H** NOS2, **I** CCDC85B, **J** ATN1

level. *In vivo* and *in vitro* validation experiments will be implemented in ongoing work.

Abbreviations

- MI Myocardial infarction
- DEGs Differentially expressed genes
- NGS Next-generation sequencing
- GEO Gene expression omnibus
- GO Gene ontology
- PPI Protein–protein interaction
- miRNA Micro-ribonucleic acid
- TF Transcription factor
- ROC Receiver operating characteristic curve

- CFTR CF transmembrane conductance regulator
- CDK1 Cyclin-dependent kinase 1
- RPS13 Ribosomal protein S13
- RPS15A Ribosomal protein S15a
- RPS27 Ribosomal protein S27
- NOTCH1 Notch receptor 1
- MRPL12 Mitochondrial ribosomal protein L12
- NOS2 Nitric oxide synthase 2
- CCDC85B Coiled-coil domain containing 85B
- ATN1 Atrophin 1

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The datasets supporting the conclusions of this article are available in the GEO (Gene Expression Omnibus) (<https://www.ncbi.nlm.nih.gov/geo/>) repository. [(GSE132143) <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE132143>].

Declarations

Ethical approval and consent to participate

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

Consent for publication

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Competing interests

The authors declare that they have no competing interests.

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