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ORIGINAL PAPER

Identification of important invasion and proliferation related genes in adrenocortical carcinoma

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Abstract

Adrenocortical carcinoma (ACC) is an end-stage hormonal syndrome. Although profound attempts have been made to illuminate the pathogenesis, the molecular mechanisms of ACC remain to be clarified. To identify the important genes in the progression of ACC, microarray datasets GSE19775 was downloaded from the gene expression omnibus database. The differentially-expressed genes (DEGs) were identified, and pathway and GO enrichment analyses were performed. The protein–protein interaction (PPI) network was constructed and the module analysis was performed using the protein interaction network analysis and Cytoscape. Also constructed target genes–miRNA regulatory network and target genes–TF regulatory network. Correlation of the hub genes were analyzed in The Cancer Genome Atlas. The prognostic values of hub genes were further validated by online tool UALCAN. Mutation analysis was done by online tool CBio Cancer Genomics Portal. A total of 884 DEGs were identified, with 441 in up regulation and 443 in down regulation. Pathways in catecholamine biosynthesis, aldosterone synthesis and secretion, pyrimidine deoxyribonucleosides salvage and systemic lupus erythematosus were the most significantly enriched for DEGs (up and down regulated). Blood vessel morphogenesis and cell cycle phase transition were the most significantly enriched term in biological processes, while extracellular matrix and chromosome, centromeric region were in cellular component and heparin binding and protein dimerization activity were in molecular function. Among the PPI networks and its module, target genes–miRNA regulatory network and target genes–TF regulatory network, hub genes were YWHAZ, FN1, GRK5, VCAM1, GATA6, TXNIP, HSPA1A, and F11R. Hub genes such as YWHAZ, STAT1, ICAM1, SH3BP5, CD83, FN1, TK1, HIST1H1C, CABLES1, and MCM3 were associated with poor overall survival, while hub genes such as STAT1, ICAM1, CD83, FN1, TK1, HIST1H1C, and MCM3 were highly expressed in stage 4. In conclusion, DEGs and hub genes diagnosed in this study may deepen our understanding of molecular mechanisms underlying the progression of ACC, and provide important targets for diagnosis and treatment of ACC.

Keywords Adrenocortical carcinoma · Bioinformatics analysis · Differentially-expressed genes · PPI network · Survival analysis

Introduction

Adrenocortical carcinoma (ACC) is rare tumor cell form in the outer layer of the adrenal gland. 0.02–0.2% ACC related deaths were reported each year in the world [1]. 5-year survival rate of ACC patients was 16–47% [2]. Due to the inadequate diagnostic methods and tools, ACC is often diagnosed at an advanced stage. Despite the key improvements in surgical treatment, the 5-year survival rate for ACC patients diagnosed with metastatic is still low at approximately 33% [3]. Thus, it's urgently needed for compassionate the molecular mechanisms of ACC progression and recognition of novel biomarkers and pathways are used for the early detection and prognosis assessment of ACC.

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Over the past decades, advance of molecular biology have increased our compassionate of the pathogenesis of ACC. Earlier researches have indicated that ACC is a genetic disease, which depends on modification of several of oncogenes and tumor suppressor genes [4]. A growing number of genes and their coding proteins related to ACC have been examined. Earlier studies reported that they play key roles in a large number of physiological and pathological processes including cell proliferation [5], differentiation [6], apoptosis [7], and metastasis [8]. However, the precise molecular mechanisms of ACC are still far from being deep understood. Newly, several studies have identified a group of ACC related candidate biomarkers and pathways by microarray analysis [9]. Genes such as PDL1 [10], IGF and IGFBP [11], TARBP2 [12], IGFII and MIB1 [13], and TOP2A [14] were responsible for pathogenesis of ACC. Pathways such as Wnt/beta-catenin pathway [15], TGF-β pathway [16], and mTOR pathway [17] were important for progression of ACC. However, few studies have assessed the key genes associated in ACC using a bioinformatics approach. Accordingly, it was crucial to explore the molecular mechanisms in ACC and to detect novel and specific biomarkers, pathways, and targets.

In this study, we have downloaded GSE19775 from gene expression omnibus (GEO) database and utilized limma R bioconductor tool to identify the DEGs between ACC and normal whole adrenal gland. Additionally, other approaches including pathway enrichment analysis from different pathway databases, Gene Ontology (GO) enrichment analysis, protein–protein interaction (PPI) network construction, submodules analysis, target genes–miRNA, interaction construction, target genes–TF interaction construction, survival analysis, and validation of hub genes. The aims of our study were to identify novel biomarkers, pathways, and potential therapeutic targets for ACC.

Materials and methods

Data collection

The gene expression profile (GSE19775) included 15 ACC samples and 15 normal whole adrenal gland samples based on platform of GPL887Agilent-012097 Human 1A Microarray (V2) G4110B (Feature Number version) was downloaded from the GEO (http://www.ncbi.nlm.nih.gov/geo/) database, which was deposited by Demeure et al. [18].

Identification of DEGs

We utilized the "limma" R bioconductor package (R Software version 3.5.2 and R Packages limma 3.38.2) [19] to screen the DEGs between ACC samples and normal whole adrenal gland samples. The FDR (false discovery rate) $P < 0.05$ and $|\log2\text{fold change (FC)}| > 1.335$ for up regulated genes and $|\log2\text{fold change (FC)}| < -0.891$ for down regulated genes were chosen as the cut-off criteria. FDR (false discovery rate) was applied to help correct false-positives.

Pathway enrichment analysis

BIOCYC (https://biocyc.org/) [20], Kyoto Encyclopedia of Genes and Genomes (KEGG) (http://www.genome.jp/kegg/pathway.html) [21], Pathway Interaction Database (PID) (https://wiki.nci.nih.gov/pages/viewpage.action?pageId=315491760) [22], REACTOME (https://reactome.org/) [23], GenMAPP (http://www.genmapp.org/) [24], MSigDB C2 BIOCARTA (v6.0) (http://software.broadinstitute.org/gsea/msigdb/collections.jsp) [25], PantherDB (http://www.pantherdb.org/) [26], Pathway Ontology (http://www.obofoundry.org/ontology/pw.html) [27], and Small Molecule Pathway Database (SMPDB) (http://smpdb.ca/) [28] were reference knowledge bases involving systems information, genomic information, and chemical information. To further explore the biological significance of DEGs, we used a online tool ToppCluster ToppCluster (https://toppcluster.cchmc.org/) [29] with the ability to analyze and visualize data to perform enrichment analysis of pathways. P value < 0.05 was considered a significant pathway enrichment.

Gene ontology (GO) enrichment analysis

Gene ontology (GO) (http://www.geneontology.org/) [30] is frequently used to annotate genes from high-throughput genome or transcriptome data. ToppCluster (https://toppcluster.cchmc.org/) [29] is an online functional annotation tool for multiple genes or proteins. P value < 0.05 was considered a significant GO enrichment.

PPI network and sub-modules analysis

Protein interaction network analysis (PINA) (http://omics.bjcancer.org/pina/home.do) [31] is an online software that contains comprehensive information of multiple proteins and is mainly used to evaluate the PPI information and this software integrates different PPI databases such as IntAct (https://www.ebi.ac.uk/intact/) [32], Molecular INTeraction Database (MINT, https://mint.bio.uniroma2.it/) [33], Biological General Repository for Interaction Datasets (BioGRID, https://thebiogrid.org/) [34], Database of Interacting Proteins (DIP, https://dip.doe-mbi.ucla.edu/dip/Main.cgi) [35], and Human Protein Reference Database (HPRD, http://www.hprd.org/) [36]. Cytoscape (http://www.cytoscape.org/) [37] version (3.7.1) was used to visualize the PPI networks of both up and down regulated genes. Confidence score ≥ 0.4 and maximum number of interactors $= 0$ were selected as the cut-off criteria. Five topological properties such as node degree [38], betweenness [39], stress [40], closeness [41], and clustering coefficient [42] were calculated in PPI networks. PEWCC1 [43] java plug-in of Cytoscape was utilized to illuminate the biological significance of gene modules in colon cancer with degree cut-off = 2, node score cut-off = 0.2, *k*-core = 2, and max. depth = 100.

Construction of target genes–miRNA regulatory network

Regulatory relationship between target genes (up and down regulated) and miRNA using online tool miRNet (https://www.mirnet.ca/) [44] which integrates 10 miRNA databases such as TarBase (http://diana.imis.athena-innovation.gr/DianaTools/index.php?r=tarbase/index) [45], miRTarBase (http://mirtarbase.mbc.nctu.edu.tw/php/download.php) [46], miRecords (http://miRecords.umn.edu/miRecords) [47], miR2Disease (http://www.mir2disease.org/) [48], HMDD (http://www.cuilab.cn/hmdd) [49], PhenomiR (http://mips.helmholtz-muenchen.de/phenomir/) [50], SM2miR (http://bioinfo.hrbmu.edu.cn/SM2miR/) [51], PharmacomiR (http://www.pharmaco-mir.org/) [52], EpimiR (http://bioinfo.hrbmu.edu.cn/EpimiR/) [53], and starBase (http://starbase.sysu.edu.cn/) [54]. Target genes–miRNA regulatory network was visualized by Cytoscape (http://www.cytoscape.org/) [37].

Construction of target genes–TF regulatory network

Regulatory relationship between target genes (up and down regulated) and TF using online tool NetworkAnalyst (https://www.networkanalyst.ca/) [55] online tool which integrates one TFs database ENCODE (https://www.encodeproject.org/pipelines/ENCPL138KID/) [56]. Target genes–TF regulatory network was visualized by Cytoscape (http://www.cytoscape.org/) [37].

Survival analysis and stage-related expression analysis of hub genes

UALCAN (http://ualcan.path.uab.edu/cgi-bin/ualcan-res.pl) [57] is an online tool for analyzing the gene expression profiles of different tumor stages and survival analysis from the Cancer Genome Atlas (TCGA). Thus, we could verify the expression levels of hub genes in all stages of ACC as well as survival analysis based on the high and low expression of hub genes in ACC. P value < 0.05 was considered as having statistical significance.

Genetical modification of hub genes

Online tool CBio Cancer Genomics Portal (http://www.cbioportal.org) [58] is an open strong platform that is use full for visualization, analysis, and downloads of large-scale cancer genomic dataset of ACC. This online tool is use full for researchers to explore and compare genetic alterations across samples.

Results

Identification of DEGs

GSE19775 dataset (15 ACC samples and 15 normal whole adrenal gland samples) were first downloaded and preprocessed (normalized) is shown in Fig. 1a and b. After preprocessing and removing batch effects, we analyzed the DEGs of GSE19775 using the limma package, using FDR (false discovery rate) $P < 0.05$ and $|\log2\text{fold change (FC)}| > 1.335$ for up regulated genes and $|\log2\text{fold change (FC)}| < -0.891$ for down regulated genes as the cut-off criterion. We screened 884 DEGs, including 441 up regulated genes and 443 down regulated genes in ACC samples compared to normal whole adrenal gland samples was shown in volcano plot (Fig. 2 and Table 1). The results of the cluster analysis of DEGs (up and down regulated) come to know that significant differences between the ACC samples and normal whole adrenal gland samples (Figs. 3 and 4).

Pathway enrichment analysis

Pathway enrichment analysis from different pathway databases (BIOCYC, KEGG, PID, REACTOME, GenMAPP, MSigDB C2 BIOCARTA, PantherDB, and SMPDB) showed that the up regulated genes were mainly associated with catecholamine biosynthesis, glucocorticoid biosynthesis, aldosterone synthesis and secretion, tyrosine metabolism, IL6-mediated signaling events, IL23-mediated signaling events, metallothioneins bind metals, metabolism of steroid hormones, steroid hormone metabolism, tyrosine metabolism, ensemble of genes encoding extracellular matrix and extracellular matrix-associated proteins, biosynthesis of neurotransmitters, Dopamine receptor mediated signaling pathway, adrenaline and noradrenaline biosynthesis, leptin system, insulin-like growth factor signaling, catecholamine biosynthesis, and steroidogenesis are listed in Table 2, mean while down regulated genes were mainly associated with pyrimidine deoxyribonucleosides salvage, glutamate removal from folates, systemic lupus erythematosus, FOXM1 transcription factor network, E2F transcription factor network, SIRT1 negatively regulates rRNA Expression, epigenetic regulation of gene expression, methionine

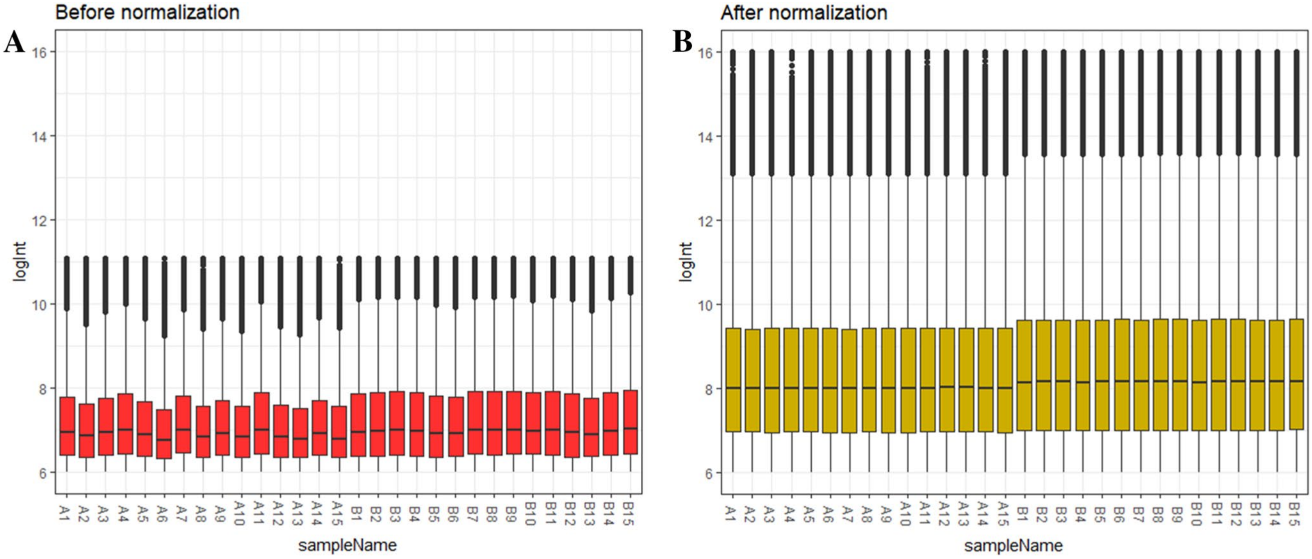


Fig. 1 Box plots of the expression profiles. A: Before normalization (red) and B: after normalization (yellow). (A1,A2, A3, A4, A5, A6, A7, A8, A9,A10, A11, A12, A13, A14, A15 = adrenocortical carcinoma samples, B1,B2, B3, B4, B5,B6, B7, B8, B9,B10, B11, B12, B13, B14, B15 = normal whole adrenal gland samples)

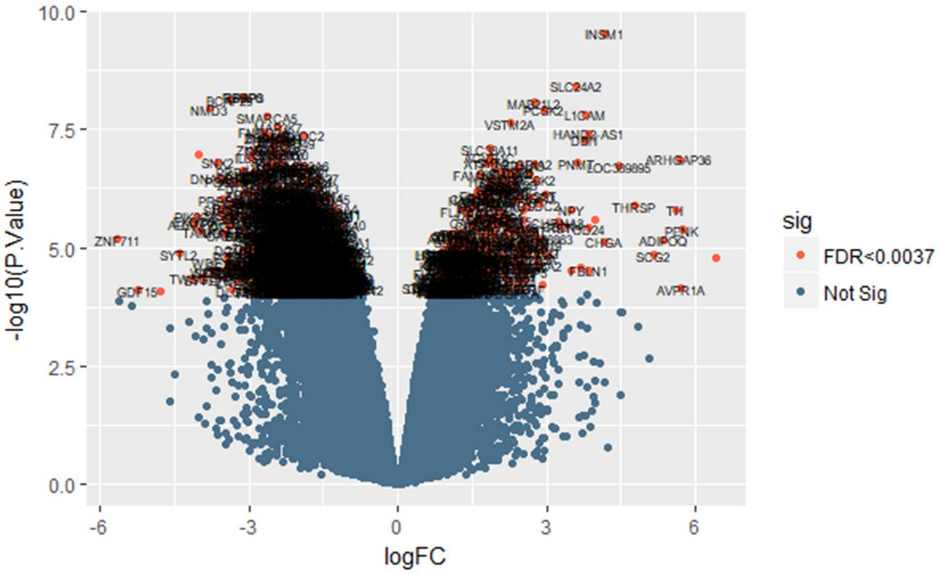


Fig. 2 A volcano plot of differentially-expressed genes

metabolism, pyrimidine metabolism, CDK Regulation of DNA Replication, ensemble of genes encoding core extracellular matrix including ECM glycoproteins, collagens and proteoglycans, integrin signaling pathway, serine glycine biosynthesis, mismatch repair pathway, nucleotide excision repair, and adenosine deaminase deficiency are listed in Table 3.

Gene ontology (GO) enrichment analysis

Gene ontology (GO) enrichment analysis from all three GO categories [biological process (BP), cellular component (CC), and molecular function (MF)] showed that the up regulated genes were mainly associated with blood vessel morphogenesis, response to other organism, extracellular matrix, extracellular space, heparin binding, and G protein-coupled receptor binding are listed in Table 4, mean while down regulated genes were mainly associated with cell cycle phase transition, negative regulation of chromosome segregation, chromosome, centromeric region, spindle, protein dimerization activity, and protein heterodimerization activity are listed in Table 5.

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

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P100642	PNMT	3.862076	5.33E−30	5.71E−26	5.71E−26	Up	Homo sapiens phenylethanolamine *N*-methyltransferase (PNMT), mRNA [NM_002686]
A_23_P254584	PENK	4.688174	5.66E−30	5.71E−26	5.71E−26	Up	Homo sapiens proenkephalin (PENK), mRNA [NM_006211]
A_23_P167493	CART	4.139177	3.83E−29	2.41E−25	2.41E−25	Up	Homo sapiens cocaine- and amphetamine-regulated transcript (CART), mRNA [NM_004291]
A_23_P14595	CHGA	3.177666	4.78E−29	2.41E−25	2.41E−25	Up	Homo sapiens chromogranin A (parathyroid secretory protein 1) (CHGA), mRNA [NM_001275]
A_23_P109287	GRIK1	2.921707	1.15E−28	4.64E−25	4.64E−25	Up	Homo sapiens glutamate receptor, ionotropic, kainate 1 (GRIK1), transcript variant 1, mRNA [NM_000830]
A_23_P217508	ZBED1	2.924317	1.99E−28	6.68E−25	6.68E−25	Up	Homo sapiens zinc finger, BED domain containing 1 (ZBED1), mRNA [NM_004729]
A_23_P51376	NKAIN1	4.655923	3.29E−28	9.48E−25	9.48E−25	Up	Sodium/potassium transporting ATPase interacting 1
A_23_P417918	PENK	2.995879	6.47E−28	1.63E−24	1.63E−24	Up	Homo sapiens proenkephalin (PENK), mRNA [NM_006211]
A_23_P117095	FGF23	1.99873	4.07E−26	9.12E−23	9.12E−23	Up	Homo sapiens fibroblast growth factor 23 (FGF23), mRNA [NM_020638]
A_23_P51132	IL1RL1	2.551372	2.39E−25	4.79E−22	4.79E−22	Up	Homo sapiens interleukin 1 receptor-like 1 (IL1RL1), transcript variant 1, mRNA [NM_016232]
A_23_P109185	INSM1	1.981731	2.61E−25	4.79E−22	4.79E−22	Up	Homo sapiens insulinoma-associated 1 (INSM1), mRNA [NM_002196]
A_23_P112296	DBH	3.032173	3.17E−25	5.33E−22	5.33E−22	Up	Homo sapiens dopamine beta-hydroxylase (dopamine beta-monooxygenase) (DBH), mRNA [NM_000787]
A_23_P93773	HOXA5	2.111467	1.31E−24	2.04E−21	2.04E−21	Up	Homo sapiens homeo box A5 (HOXA5), mRNA [NM_019102]
A_23_P202245	M31213	2.885334	2.83E−24	4.08E−21	4.08E−21	Up	Human papillary thyroid carcinoma-encoded protein mRNA, complete cds. [M31213]
A_23_P154115	IGFBP5	2.153061	4.43E−24	5.96E−21	5.96E−21	Up	Homo sapiens insulin-like growth factor binding protein 5 (IGFBP5), mRNA [NM_000599]
A_23_P213228	PHOX2B	2.107813	1.35E−23	1.7E−20	1.7E−20	Up	Homo sapiens paired-like homeobox 2b (PHOX2B), mRNA [NM_003924]
A_23_P38628	#N/A	1.728791	1.02E−22	1.17E−19	1.17E−19	Up	Unknown
A_23_P21770	SLC18A1	1.541591	1.04E−22	1.17E−19	1.17E−19	Up	Homo sapiens solute carrier family 18 (vesicular monoamine), member 1 (SLC18A1), mRNA [NM_003053]
A_23_P145104	TFAP2B	2.187323	1.45E−22	1.54E−19	1.54E−19	Up	Homo sapiens transcription factor AP-2 beta (activating enhancer binding protein 2 beta) (TFAP2B), mRNA [NM_003221]
A_23_P433050	LGR7	1.605385	4.19E−22	4.22E−19	4.22E−19	Up	Homo sapiens leucine-rich repeat-containing G protein-coupled receptor 7 (LGR7), mRNA [NM_021634]
A_23_P37251	SNAPC1	1.565012	8.5E−22	8.17E−19	8.17E−19	Up	Homo sapiens small nuclear RNA activating complex, polypeptide 1, 43 kDa (SNAPC1), mRNA [NM_003082]
A_23_P377296	ECE2	2.446848	9.74E−22	8.93E−19	8.93E−19	Up	Homo sapiens endothelin converting enzyme 2 (ECE2), mRNA [NM_014693]
A_23_P12874	GTPBP4	2.95776	1.11E−21	9.64E−19	9.64E−19	Up	Homo sapiens GTP binding protein 4 (GTPBP4), mRNA [NM_012341]
A_23_P50376	ZNF331	1.927253	1.15E−21	9.64E−19	9.64E−19	Up	Homo sapiens zinc finger protein 331 (ZNF331), mRNA [NM_018555]
A_23_P159488	#N/A	1.935488	1.74E−21	1.4E−18	1.4E−18	Up	Unknown
A_23_P31755	CRH	1.733868	6.49E−21	5.04E−18	5.04E−18	Up	Homo sapiens corticotropin releasing hormone (CRH), mRNA [NM_000756]
A_23_P127220	DNAJC12	3.19852	8.37E−21	6.26E−18	6.26E−18	Up	Homo sapiens DnaJ (Hsp40) homolog, subfamily C, member 12 (DNAJC12), transcript variant 1, mRNA [NM_021800]
A_23_P107201	STAT3	1.583632	1.31E−20	9.45E−18	9.45E−18	Up	Homo sapiens signal transducer and activator of transcription 3 (acute-phase response factor) (STAT3), transcript variant 1, mRNA [NM_139276]
A_23_P397969	FOXK2	1.418692	1.6E−20	1.08E−17	1.08E−17	Up	Homo sapiens forkhead box K2 (FOXK2), transcript variant 2, mRNA [NM_181430]
A_23_P55036	#N/A	2.015147	1.6E−20	1.08E−17	1.08E−17	Up	Unknown
A_23_P95891	TH	1.370203	2.07E−20	1.35E−17	1.35E−17	Up	Homo sapiens tyrosine hydroxylase (TH), transcript variant 3, mRNA [NM_199293]
A_23_P16834	FNDC4	2.092442	2.89E−20	1.82E−17	1.82E−17	Up	Homo sapiens fibronectin type III domain containing 4 (FNDC4), mRNA [NM_022823]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P375404	SLC25A19	1.924395	3.97E−20	2.43E−17	2.43E−17	Up	Homo sapiens solute carrier family 25 (mitochondrial deoxynucleotide carrier), member 19 (SLC25A19), mRNA [NM_021734]
A_23_P74508	THC2132706	1.922996	5.36E−20	3.18E−17	3.18E−17	Up	Q92681 (Q92681) Sodium-D-glucose cotransporter, complete [THC2132706]
A_23_P209861	TLX2	1.935797	7.24E−20	4.17E−17	4.17E−17	Up	T-cell leukemiahomeobox protein 2 (Homeobox protein Hox-11L1) (Neural crest homeobox protein). [Source:Uniprot/SWISSPROT;Acc:O43763] [ENST00000233638]
A_23_P10062	HGNT-IV-H	1.470712	1.7E−19	9.51E−17	9.51E−17	Up	Homo sapiens UDP-*N*-acetylglucosamine:a-1,3-D-mannoside beta-1,4-*N*-acetylglucosaminyltransferase IV (HGNT-IV-H), mRNA [NM_013244]
A_23_P433690	ZNF331	2.519599	2.33E−19	1.27E−16	1.27E−16	Up	Homo sapiens zinc finger protein 331 (ZNF331), mRNA [NM_018555]
A_23_P104579	DOC-1R	1.417013	6.1E−19	3.15E−16	3.15E−16	Up	Homo sapiens tumor suppressor deleted in oral cancer-related 1 (DOC-1R), mRNA [NM_005851]
A_23_P369479	MSI2	1.767271	6.28E−19	3.17E−16	3.17E−16	Up	Homo sapiens musashi homolog 2 (Drosophila) (MSI2), transcript variant 2, mRNA [NM_170721]
A_23_P36962	DNAJC3	1.722278	1.08E−18	5.16E−16	5.16E−16	Up	Homo sapiens DnaJ (Hsp40) homolog, subfamily C, member 3 (DNAJC3), mRNA [NM_006260]
A_23_P138218	FMO2	1.612474	1.1E−18	5.16E−16	5.16E−16	Up	Dimethylanilinemonooxygenase [*N*-oxide-forming] 2 (EC 1.14.13.8) (Pulmonary flavin-containing monooxygenase 2) (FMO 2) (Dimethylaniline oxidase 2) (FMO 1B1). [Source:Uniprot/SWISSPROT;Acc:Q99518] [ENST00000209929]
A_23_P126103	CTH	3.881723	1.27E−18	5.84E−16	5.84E−16	Up	Homo sapiens cystathionase (cystathionine gamma-lyase) (CTH), transcript variant 1, mRNA [NM_001902]
A_23_P56433	ECRG4	2.036224	1.3E−18	5.85E−16	5.85E−16	Up	Homo sapiens esophageal cancer-related gene 4 protein (ECRG4), mRNA [NM_032411]
A_23_P356616	ABTB2	1.727396	1.37E−18	5.91E−16	5.91E−16	Up	Homo sapiens ankyrin repeat and BTB (POZ) domain containing 2 (ABTB2), mRNA [NM_145804]
A_23_P209559	REG-III	2.489493	2.11E−18	8.86E−16	8.86E−16	Up	Homo sapiens LPPM429 (REG-III), mRNA [NM_198448]
A_23_P162640	GABARAPL1	1.690806	2.2E−18	9.08E−16	9.08E−16	Up	Homo sapiens GABA(A) receptor-associated protein-like 1 (GABARAPL1), mRNA [NM_031412]
A_23_P73451	#N/A	2.111801	3.1E−18	1.2E−15	1.2E−15	Up	Unknown
A_23_P21462	HGNT-IV-H	1.368797	3.43E−18	1.31E−15	1.31E−15	Up	Homo sapiens UDP-*N*-acetylglucosamine:a-1,3-D-mannoside beta-1,4-*N*-acetylglucosaminyltransferase IV (HGNT-IV-H), mRNA [NM_013244]
A_23_P54992	Dlc2	1.506813	3.78E−18	1.41E−15	1.41E−15	Up	Homo sapiens dynein light chain 2 (Dlc2), mRNA [NM_080677]
A_23_P212119	GALNTL2	1.5049	4.53E−18	1.66E−15	1.66E−15	Up	Homo sapiens UDP-*N*-acetyl-alpha-D-galactosamine:polypeptide-*N*-acetylgalactosaminyltransferase-like 2 (GALNTL2), mRNA [NM_054110]
A_23_P200780	TGFBR3	2.025546	5.21E−18	1.88E−15	1.88E−15	Up	Homo sapiens transforming growth factor, beta receptor III (betaglycan, 300 kDa) (TGFBR3), mRNA [NM_003243]
A_23_P86706	ZRANB1	1.546621	7.82E−18	2.67E−15	2.67E−15	Up	Homo sapiens zinc finger, RAN-binding domain containing 1, mRNA (cDNA clone IMAGE:5188569), complete cds. [BC048281]
A_23_P208031	SYT4	3.304125	8.22E−18	2.77E−15	2.77E−15	Up	Homo sapiens synaptotagmin IV (SYT4), mRNA [NM_020783]
A_23_P143973	SH3BP5	2.351507	8.65E−18	2.86E−15	2.86E−15	Up	Homo sapiens SH3-domain binding protein 5 (BTK-associated) (SH3BP5), mRNA [NM_004844]
A_23_P216877	NR4A3	2.219885	1.29E−17	4.12E−15	4.12E−15	Up	Homo sapiens nuclear receptor subfamily 4, group A, member 3 (NR4A3), transcript variant 2, mRNA [NM_173198]
A_23_P304554	MRAP	1.910565	1.47E−17	4.63E−15	4.63E−15	Up	Homo sapiens chromosome 21 open reading frame 61 (C21orf61), transcript variant 2, mRNA [NM_206898]
A_23_P41188	MRAS	2.028819	1.53E−17	4.73E−15	4.73E−15	Up	Homo sapiens muscle RAS oncogene homolog (MRAS), mRNA [NM_012219]
A_23_P97309	CASP9	2.047753	1.55E−17	4.73E−15	4.73E−15	Up	Homo sapiens caspase 9, apoptosis-related cysteine protease (CASP9), transcript variant alpha, mRNA [NM_001229]
A_23_P337849	TNRC4	1.584793	1.61E−17	4.85E−15	4.85E−15	Up	Homo sapiens trinucleotide repeat-containing 4 (TNRC4), mRNA [NM_007185]
A_23_P377197	MRAS	1.356469	1.67E−17	4.95E−15	4.95E−15	Up	Homo sapiens muscle RAS oncogene homolog (MRAS), mRNA [NM_012219]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P201979	CREM	2.693538	1.78E−17	5.22E−15	5.22E−15	Up	Homo sapiens cAMP responsive element modulator (CREM), transcript variant 19, mRNA [NM_183013]
A_23_P38649	MC2R	1.756479	1.84E−17	5.23E−15	5.23E−15	Up	Homo sapiens melanocortin 2 receptor (adrenocorticotropic hormone) (MC2R), mRNA [NM_000529]
A_23_P107581	NPC1	2.143887	1.98E−17	5.51E−15	5.51E−15	Up	Homo sapiens Niemann-Pick disease, type C1 (NPC1), mRNA [NM_000271]
A_23_P98022	SIRT1	1.761612	2.02E−17	5.51E−15	5.51E−15	Up	Homo sapiens sirtuin (silent mating type information regulation 2 homolog) 1 (S. cerevisiae) (SIRT1), mRNA [NM_012238]
A_23_P68007	ATP1B3	2.347276	2.21E−17	5.93E−15	5.93E−15	Up	Homo sapiens ATPase, Na+/K+transporting, beta 3 polypeptide (ATP1B3), mRNA [NM_001679]
A_23_P139216	H19	2.125771	2.77E−17	7.31E−15	7.31E−15	Up	Homo sapiens H19, imprinted maternally expressed untranslated mRNA (H19) on chromosome 11 [NR_002196]
A_23_P319423	KCNK5	1.805423	2.79E−17	7.31E−15	7.31E−15	Up	Homo sapiens potassium channel, subfamily K, member 5 (KCNK5), mRNA [NM_003740]
A_23_P71530	TNFRSF11B	1.802029	3.36E−17	8.7E−15	8.7E−15	Up	Homo sapiens tumor necrosis factor receptor superfamily, member 11b (osteoprotegerin) (TNFRSF11B), mRNA [NM_002546]
A_23_P165598	ENST00000309950	3.920316	3.46E−17	8.73E−15	8.73E−15	Up	Homo sapiens full-length insert cDNA clone ZE09G12. [AF086541]
A_23_P253911	CHRNA3	3.423152	6.16E−17	1.53E−14	1.53E−14	Up	Homo sapiens cholinergic receptor, nicotinic, alpha polypeptide 3 (CHRNA3), mRNA [NM_000743]
A_23_P145644	DDC	2.929227	7.92E−17	1.95E−14	1.95E−14	Up	Homo sapiens dopa decarboxylase (aromatic L-amino acid decarboxylase) (DDC), mRNA [NM_000790]
A_23_P134953	ADFP	2.515094	9.47E−17	2.28E−14	2.28E−14	Up	Homo sapiens adipose differentiation-related protein (ADFP), mRNA [NM_001122]
A_23_P65817	GABARAPL1	1.443124	1.36E−16	3.15E−14	3.15E−14	Up	Homo sapiens GABA(A) receptor-associated protein-like 1 (GABARAPL1), mRNA [NM_031412]
A_23_P105963	AK7	1.360386	1.49E−16	3.41E−14	3.41E−14	Up	Homo sapiens adenylate kinase 7 (AK7), mRNA [NM_152327]
A_23_P54267	SCG3	2.509971	1.84E−16	4.17E−14	4.17E−14	Up	Homo sapiens secretogranin III (SCG3), mRNA [NM_013243]
A_23_P364517	SELK	1.677093	2.08E−16	4.62E−14	4.62E−14	Up	Homo sapiens selenoprotein K (SELK), mRNA [NM_021237]
A_23_P73517	CITED1	2.737499	2.12E−16	4.65E−14	4.65E−14	Up	Homo sapiens Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 1 (CITED1), mRNA [NM_004143]
A_23_P127851	FXC1	1.641758	2.49E−16	5.35E−14	5.35E−14	Up	Homo sapiens fracture callus 1 homolog (rat) (FXC1), mRNA [NM_012192]
A_23_P75622	ATP5L	1.748406	2.6E−16	5.46E−14	5.46E−14	Up	Homo sapiens ATP synthase, H+transporting, mitochondrial F0 complex, subunit g (ATP5L), nuclear gene encoding mitochondrial protein, mRNA [NM_006476]
A_23_P355295	FMO2	2.497087	3.31E−16	6.84E−14	6.84E−14	Up	Homo sapiens flavin-containing monooxygenase 2 (FMO2), mRNA [NM_001460]
A_23_P76644	RAB20	1.76003	3.77E−16	7.6E−14	7.6E−14	Up	Homo sapiens RAB20, member RAS oncogene family (RAB20), mRNA [NM_017817]
A_23_P6951	ATP1B3	2.41136	4.22E−16	8.34E−14	8.34E−14	Up	Homo sapiens ATPase, Na+/K+transporting, beta 3 polypeptide (ATP1B3), mRNA [NM_001679]
A_23_P125788	TCEAL7	2.138833	4.53E−16	8.81E−14	8.81E−14	Up	Homo sapiens transcription elongation factor A (SII)-like 7 (TCEAL7), mRNA [NM_152278]
A_23_P101992	MARCO	1.783161	4.54E−16	8.81E−14	8.81E−14	Up	Homo sapiens macrophage receptor with collagenous structure (MARCO), mRNA [NM_006770]
A_23_P72097	AK124258	1.364451	4.72E−16	9.07E−14	9.07E−14	Up	Homo sapiens cDNA FLJ42264 fis, clone TKIDN2014757. [AK124258]
A_23_P369201	SCARB1	2.172387	5.21E−16	9.91E−14	9.91E−14	Up	Homo sapiens scavenger receptor class B, member 1 (SCARB1), mRNA [NM_005505]
A_23_P68970	ARFGAP3	2.020777	5.77E−16	1.09E−13	1.09E−13	Up	Homo sapiens ADP-ribosylation factor GTPase activating protein 3 (ARFGAP3), mRNA [NM_014570]
A_23_P121064	PTX3	2.4986	6.1E−16	1.13E−13	1.13E−13	Up	Homo sapiens pentaxin-related gene, rapidly induced by IL-1 beta (PTX3), mRNA [NM_002852]
A_23_P112982	DKFZp761H039	1.503605	6.13E−16	1.13E−13	1.13E−13	Up	Homo sapiens hypothetical protein DKFZp761H039 (DKFZp761H039), mRNA [NM_018711]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P255231	TNFAIP9	1.577255	7.53E−16	1.38E−13	1.38E−13	Up	Homo sapiens tumor necrosis factor, alpha-induced protein 9 (TNFAIP9), mRNA [NM_024636]
A_23_P80570	AADAC	3.25721	9.13E−16	1.62E−13	1.62E−13	Up	Homo sapiens arylacetamidedeacetylase (esterase) (AADAC), mRNA [NM_001086]
A_23_P207481	PRO1855	1.725648	1.22E−15	2.1E−13	2.1E−13	Up	Homo sapiens hypothetical protein PRO1855 (PRO1855), mRNA [NM_018509]
A_23_P129896	ALDH3A2	1.790667	1.49E−15	2.44E−13	2.44E−13	Up	Homo sapiens aldehyde dehydrogenase 3 family, member A2 (ALDH3A2), mRNA [NM_000382]
A_23_P95690	SPOCK3	1.884998	1.72E−15	2.76E−13	2.76E−13	Up	Homo sapiens sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 3, mRNA (cDNA clone MGC:20285 IMAGE:4110883), complete cds. [BC013983]
A_23_P133000	FLJ11539	1.760181	2.07E−15	3.22E−13	3.22E−13	Up	Homo sapiens cDNA FLJ11539 fis, clone HEMBA1002748. [AK021601]
A_23_P67008	GATA6	1.405279	2.77E−15	4.1E−13	4.1E−13	Up	H.sapiens mRNA for GATA-6 DNA binding protein. [X95701]
A_23_P168598	PON1	3.047742	2.85E−15	4.16E−13	4.16E−13	Up	Homo sapiens paraoxonase 1 (PON1), mRNA [NM_000446]
A_23_P436259	ERN1	2.753	4.09E−15	5.78E−13	5.78E−13	Up	Homo sapiens endoplasmic reticulum to nucleus signaling 1 (ERN1), transcript variant 2, mRNA [NM_152461]
A_23_P96590	GPRASP1	2.078982	4.12E−15	5.78E−13	5.78E−13	Up	Homo sapiens G protein-coupled receptor-associated sorting protein 1 (GPRASP1), mRNA [NM_014710]
A_23_P42257	IER3	2.63007	4.33E−15	6.03E−13	6.03E−13	Up	Homo sapiens immediate early response 3 (IER3), transcript variant short, mRNA [NM_003897]
A_23_P113121	DLG2	1.415549	6.21E−15	8.35E−13	8.35E−13	Up	Homo sapiens cDNA FLJ44824 fis, clone BRACE3046491, highly similar to Channel associated protein of synapse-110. [AK126776]
A_23_P357207	C6orf117	1.68629	6.37E−15	8.51E−13	8.51E−13	Up	Homo sapiens chromosome 6 open reading frame 117 (C6orf117), mRNA [NM_138409]
A_23_P503200	PHF10	1.596555	7.65E−15	1E−12	1E−12	Up	Homo sapiens PHD finger protein 10 (PHF10), transcript variant 1, mRNA [NM_018288]
A_23_P118392	RASD1	2.744722	8.56E−15	1.11E−12	1.11E−12	Up	Homo sapiens RAS, dexamethasone-induced 1 (RASD1), mRNA [NM_016084]
A_23_P84118	CDH18	1.98853	1.04E−14	1.34E−12	1.34E−12	Up	Homo sapiens cadherin 18, type 2 (CDH18), mRNA [NM_004934]
A_23_P218331	CYB561	1.520825	1.14E−14	1.45E−12	1.45E−12	Up	Homo sapiens cytochrome b-561 (CYB561), mRNA [NM_001915]
A_23_P343671	FOSL2	1.725996	1.18E−14	1.5E−12	1.5E−12	Up	Fos-related antigen 2. [Source:Uniprot/SWISSPROT;Acc:P15408] [ENST00000265539]
A_23_P140469	H63	1.340076	1.22E−14	1.54E−12	1.54E−12	Up	Homo sapiens H63 breast cancer expressed gene (H63), transcript variant 1, mRNA [NM_138423]
A_23_P49610	MGC14376	2.58376	1.5E−14	1.85E−12	1.85E−12	Up	Homo sapiens hypothetical protein MGC14376 (MGC14376), transcript variant 1, mRNA [NM_032895]
A_23_P167328	CD38	1.845708	1.59E−14	1.96E−12	1.96E−12	Up	Homo sapiens CD38 antigen (p45) (CD38), mRNA [NM_001775]
A_23_P118552	HIS1	2.348217	1.74E−14	2.12E−12	2.12E−12	Up	Homo sapiens HMBA-inducible (HIS1), mRNA [NM_006460]
A_23_P114708	CYP4B1	2.210782	2.04E−14	2.43E−12	2.43E−12	Up	Homo sapiens cytochrome P450, family 4, subfamily B, polypeptide 1 (CYP4B1), mRNA [NM_000779]
A_23_P20022	HIG2	2.444495	2.1E−14	2.49E−12	2.49E−12	Up	Homo sapiens hypoxia-inducible protein 2 (HIG2), mRNA [NM_013332]
A_23_P7154	HAND2	1.92027	2.18E−14	2.57E−12	2.57E−12	Up	Heart- and neural crest derivatives-expressed protein 2 (Deciduum, heart, autonomic nervous system and neural crest derivatives-expressed protein 2) (dHAND). [Source:Uniprot/SWISSPROT;Acc:P61296] [ENST00000359562]
A_23_P397455	ACVR1C	1.939107	2.43E−14	2.84E−12	2.84E−12	Up	Homo sapiens activin A receptor, type IC (ACVR1C), mRNA [NM_145259]
A_23_P150693	FJX1	1.402416	2.5E−14	2.89E−12	2.89E−12	Up	Homo sapiens four jointed box 1 (Drosophila) (FJX1), mRNA [NM_014344]
A_23_P213857	C7	1.848636	2.51E−14	2.89E−12	2.89E−12	Up	Homo sapiens complement component 7 (C7), mRNA [NM_000587]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P132718	SEMA3B	1.962079	3.26E−14	3.7E−12	3.7E−12	Up	Homo sapiens sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B (SEMA3B), transcript variant 1, mRNA [NM_004636]
A_23_P151525	C14orf132	2.397073	3.52E−14	3.97E−12	3.97E−12	Up	Homo sapiens mRNA; cDNA DKFZp761F2014 (from clone DKFZp761F2014). [AL390130]
A_23_P129167	CYP11A1	2.304998	4.02E−14	4.43E−12	4.43E−12	Up	Homo sapiens cytochrome P450, family 11, subfamily A, polypeptide 1 (CYP11A1), nuclear gene encoding mitochondrial protein, mRNA [NM_000781]
A_23_P33803	C15orf12	1.512273	4.16E−14	4.56E−12	4.56E−12	Up	Homo sapiens chromosome 15 open reading frame 12 (C15orf12), nuclear gene encoding mitochondrial protein, mRNA [NM_018285]
A_23_P19134	MASS1	2.447198	4.19E−14	4.57E−12	4.57E−12	Up	Homo sapiens monogenic, audiogenic seizure susceptibility 1 homolog (mouse) (MASS1), mRNA [NM_032119]
A_23_P319005	HMP19	1.407011	4.44E−14	4.79E−12	4.79E−12	Up	Homo sapiens HMP19 protein (HMP19), mRNA [NM_015980]
A_23_P107283	HOXB2	3.312435	4.64E−14	4.95E−12	4.95E−12	Up	Homo sapiens homeo box B2 (HOXB2), mRNA [NM_002145]
A_23_P162162	KCTD14	1.481675	4.93E−14	5.15E−12	5.15E−12	Up	Homo sapiens potassium channel tetramerisation domain containing 14 (KCTD14), mRNA [NM_023930]
A_23_P331598	IPO7	1.581736	5.11E−14	5.31E−12	5.31E−12	Up	Homo sapiens importin 7 (IPO7), mRNA [NM_006391]
A_23_P8812	W60781	4.591366	5.48E−14	5.64E−12	5.64E−12	Up	W60781 zd26f05.r1 Soares_fetal_heart_NbHH19 W Homo sapiens cDNA clone IMAGE:341793 5′ similar to gb:J02874 FATTY ACID-BINDING PROTEIN, ADIPOCYTE (HUMAN);, mRNA sequence [W60781]
A_23_P252825	SCAP	1.623357	6.82E−14	6.88E−12	6.88E−12	Up	Homo sapiens SREBP cleavage-activating protein (SCAP), mRNA [NM_012235]
A_23_P210100	CYP26B1	2.77758	7.02E−14	7.05E−12	7.05E−12	Up	Homo sapiens cytochrome P450, family 26, subfamily B, polypeptide 1 (CYP26B1), mRNA [NM_019885]
A_23_P79191	SCG2	2.323298	7.43E−14	7.39E−12	7.39E−12	Up	Homo sapiens secretogranin II (chromogranin C) (SCG2), mRNA [NM_003469]
A_23_P351724	TNS	1.597581	8.11E−14	7.96E−12	7.96E−12	Up	Homo sapiens tensin (TNS), mRNA [NM_022648]
A_23_P258944	DNAJB9	2.111099	8.13E−14	7.96E−12	7.96E−12	Up	Homo sapiens DnaJ (Hsp40) homolog, subfamily B, member 9 (DNAJB9), mRNA [NM_012328]
A_23_P7144	CXCL1	4.170018	8.34E−14	8.09E−12	8.09E−12	Up	Homo sapiens chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha) (CXCL1), mRNA [NM_001511]
A_23_P33356	ADAMTS9	1.476219	9.52E−14	9.15E−12	9.15E−12	Up	Homo sapiens a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 9 (ADAMTS9), transcript variant 3, mRNA [NM_020249]
A_23_P96556	GK	1.577488	1.02E−13	9.71E−12	9.71E−12	Up	Homo sapiens glycerol kinase (GK), transcript variant 2, mRNA [NM_000167]
A_23_P97173	HSD3B1	2.079204	1.05E−13	9.93E−12	9.93E−12	Up	Homo sapiens hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1 (HSD3B1), mRNA [NM_000862]
A_23_P64617	FZD4	2.4913	1.09E−13	1.01E−11	1.01E−11	Up	Homo sapiens frizzled homolog 4 (Drosophila) (FZD4), mRNA [NM_012193]
A_23_P119882	GCKR	2.32016	1.15E−13	1.07E−11	1.07E−11	Up	Homo sapiens glucokinase (hexokinase 4) regulator (GCKR), mRNA [NM_001486]
A_23_P90649	IRS1	1.755175	1.19E−13	1.1E−11	1.1E−11	Up	Homo sapiens insulin receptor substrate 1 (IRS1), mRNA [NM_005544]
A_23_P78998	C19orf4	1.675145	1.34E−13	1.23E−11	1.23E−11	Up	Homo sapiens chromosome 19 open reading frame 4, mRNA (cDNA clone MGC:17013 IMAGE:4181442), complete cds. [BC010446]
A_23_P318220	SF1	1.44619	1.42E−13	1.28E−11	1.28E−11	Up	Homo sapiens splicing factor 1 (SF1), transcript variant 1, mRNA [NM_004630]
A_23_P170719	#N/A	2.232912	1.49E−13	1.32E−11	1.32E−11	Up	Unknown
A_23_P216756	FCN2	2.26708	2.21E−13	1.9E−11	1.9E−11	Up	Homo sapiens ficolin (collagen/fibrinogen domain containing lectin) 2 (hucolin) (FCN2), transcript variant SV2, mRNA [NM_015838]
A_23_P19592	PGM3	1.906372	2.26E−13	1.93E−11	1.93E−11	Up	Homo sapiens phosphoglucomutase 3 (PGM3), mRNA [NM_015599]
A_23_P51576	HSD3B2	2.371733	2.33E−13	1.98E−11	1.98E−11	Up	Homo sapiens hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2 (HSD3B2), mRNA [NM_000198]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P132793	ARMET	1.338678	2.71E−13	2.29E−11	2.29E−11	Up	Homo sapiens arginine-rich, mutated in early stage tumors (ARMET), mRNA [NM_006010]
A_23_P46673	PTP4A1P7	1.909126	2.79E−13	2.34E−11	2.34E−11	Up	Protein tyrosine phosphatase type IVA, member 1 pseudogene 7
A_23_P20494	NDRG1	1.617446	2.87E−13	2.4E−11	2.4E−11	Up	Homo sapiens N-myc downstream regulated gene 1 (NDRG1), mRNA [NM_006096]
A_23_P11685	PLA2G4A	1.66679	2.94E−13	2.45E−11	2.45E−11	Up	Homo sapiens phospholipase A2, group IVA (cytosolic, calcium-dependent) (PLA2G4A), mRNA [NM_024420]
A_23_P340848	PTGIR	1.337042	2.98E−13	2.47E−11	2.47E−11	Up	Homo sapiens prostaglandin I2 (prostacyclin) receptor (IP) (PTGIR), mRNA [NM_000960]
A_23_P107117	ZNF179	2.033328	3.02E−13	2.48E−11	2.48E−11	Up	Homo sapiens zinc finger protein 179 (ZNF179), mRNA [NM_007148]
A_23_P45699	FUBP1	1.513442	3.02E−13	2.48E−11	2.48E−11	Up	Homo sapiens far upstream element (FUSE) binding protein 1 (FUBP1), mRNA [NM_003902]
A_23_P348121	FOSL2	1.569973	3.03E−13	2.49E−11	2.49E−11	Up	Homo sapiens FOS-like antigen 2 (FOSL2), mRNA [NM_005253]
A_23_P128246	HYPE	1.399506	3.28E−13	2.66E−11	2.66E−11	Up	Homo sapiens Huntingtin interacting protein E (HYPE), mRNA [NM_007076]
A_23_P139669	SLC2A3	1.531093	3.62E−13	2.92E−11	2.92E−11	Up	Homo sapiens solute carrier family 2 (facilitated glucose transporter), member 3 (SLC2A3), mRNA [NM_006931]
A_23_P56488	FLJ39822	1.574817	3.92E−13	3.12E−11	3.12E−11	Up	Homo sapiens hypothetical protein FLJ39822 (FLJ39822), mRNA [NM_173512]
A_23_P14026	CREBL2	1.920481	4.37E−13	3.44E−11	3.44E−11	Up	Homo sapiens cAMP responsive element binding protein-like 2 (CREBL2), mRNA [NM_001310]
A_23_P103877	LRRC38	2.905012	4.44E−13	3.49E−11	3.49E−11	Up	leucine-rich repeat-containing 38
A_23_P131207	NR4A2	2.936932	4.47E−13	3.49E−11	3.49E−11	Up	Homo sapiens nuclear receptor subfamily 4, group A, member 2 (NR4A2), transcript variant 1, mRNA [NM_006186]
A_23_P169178	TESK1	1.743538	5.17E−13	4.01E−11	4.01E−11	Up	Homo sapiens testis-specific kinase 1 (TESK1), mRNA [NM_006285]
A_23_P207221	FLJ10847	1.945659	5.89E−13	4.54E−11	4.54E−11	Up	Homo sapiens hypothetical protein FLJ10847 (FLJ10847), mRNA [NM_018242]
A_23_P64721	GPR109B	1.444271	6.47E−13	4.95E−11	4.95E−11	Up	Homo sapiens G protein-coupled receptor 109B (GPR109B), mRNA [NM_006018]
A_23_P128520	IGFBP6	1.343894	7.1E−13	5.34E−11	5.34E−11	Up	Homo sapiens insulin-like growth factor binding protein 6 (IGFBP6), mRNA [NM_002178]
A_23_P398566	NR4A3	3.507994	8.02E−13	5.99E−11	5.99E−11	Up	Homo sapiens nuclear receptor subfamily 4, group A, member 3 (NR4A3), transcript variant 3, mRNA [NM_173200]
A_23_P69699	NPY1R	3.07192	8.28E−13	6.14E−11	6.14E−11	Up	Homo sapiens neuropeptide Y receptor Y1 (NPY1R), mRNA [NM_000909]
A_23_P251841	NRXN3	1.541648	1.05E−12	7.58E−11	7.58E−11	Up	Homo sapiens neurexin 3 (NRXN3), transcript variant alpha, mRNA [NM_004796]
A_23_P91919	SERP1	1.565086	1.18E−12	8.49E−11	8.49E−11	Up	Homo sapiens stress-associated endoplasmic reticulum protein 1 (SERP1), mRNA [NM_014445]
A_23_P64138	ST3GAL4	1.663446	1.3E−12	9.25E−11	9.25E−11	Up	Homo sapiens sialyltransferase 4C (beta-galactoside alpha-2,3-sialyltransferase) (SIAT4C), mRNA [NM_006278]
A_23_P161659	SYT13	1.526182	1.31E−12	9.29E−11	9.29E−11	Up	Homo sapiens synaptotagmin XIII (SYT13), mRNA [NM_020826]
A_23_P110941	GSTA4	2.268318	1.33E−12	9.33E−11	9.33E−11	Up	Homo sapiens glutathione S-transferase A4 (GSTA4), mRNA [NM_001512]
A_23_P811	G1P2	2.22658	1.49E−12	1.03E−10	1.03E−10	Up	Homo sapiens interferon, alpha-inducible protein (clone IFI-15K), mRNA (cDNA clone MGC:3945 IMAGE:3545944), complete cds. [BC009507]
A_23_P69208	TIMP4	3.009632	1.5E−12	1.03E−10	1.03E−10	Up	Homo sapiens tissue inhibitor of metalloproteinase 4 (TIMP4), mRNA [NM_003256]
A_23_P128166	RAB21	1.766947	1.96E−12	1.29E−10	1.29E−10	Up	Homo sapiens RAB21, member RAS oncogene family (RAB21), mRNA [NM_014999]
A_23_P382584	CHGB	4.047818	2.1E−12	1.37E−10	1.37E−10	Up	Homo sapiens chromogranin B (secretogranin 1) (CHGB), mRNA [NM_001819]
A_23_P203751	FLJ22104	1.343773	2.17E−12	1.42E−10	1.42E−10	Up	Homo sapiens hypothetical protein FLJ22104 (FLJ22104), mRNA [NM_022918]
A_23_P215997	CYP11B2	2.622082	2.66E−12	1.71E−10	1.71E−10	Up	Homo sapiens cytochrome P450, family 11, subfamily B, polypeptide 2 (CYP11B2), nuclear gene encoding mitochondrial protein, mRNA [NM_000498]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P60166	DEPDC6	1.824423	2.81E−12	1.8E−10	1.8E−10	Up	Homo sapiens DEP domain containing 6 (DEPDC6), mRNA [NM_022783]
A_23_P81006	IL8	1.648247	2.92E−12	1.86E−10	1.86E−10	Up	Homo sapiens interleukin 8 (IL8), mRNA [NM_000584]
A_23_P41645	ELL2	2.322971	3.03E−12	1.91E−10	1.91E−10	Up	Homo sapiens elongation factor, RNA polymerase II, 2 (ELL2), mRNA [NM_012081]
A_23_P126486	MGC12760	1.697577	3.58E−12	2.22E−10	2.22E−10	Up	Homo sapiens hypothetical protein MGC12760, mRNA (cDNA clone MGC:12760 IMAGE:4111573), complete cds. [BC006312]
A_23_P109427	GSTT2	2.430491	3.64E−12	2.25E−10	2.25E−10	Up	Homo sapiens glutathione S-transferase theta 2 (GSTT2), mRNA [NM_000854]
A_23_P401568	MAT2A	1.790256	3.71E−12	2.27E−10	2.27E−10	Up	Homo sapiens methionine adenosyltransferase II, alpha (MAT2A), mRNA [NM_005911]
A_23_P136978	SRPX2	1.87333	4E−12	2.44E−10	2.44E−10	Up	Homo sapiens sushi-repeat-containing protein, X-linked 2 (SRPX2), mRNA [NM_014467]
A_23_P162068	SLC1A2	2.628632	4.91E−12	2.94E−10	2.94E−10	Up	Homo sapiens solute carrier family 1 (glial high affinity glutamate transporter), member 2 (SLC1A2), mRNA [NM_004171]
A_23_P364544	C12ORF60	1.378707	5.25E−12	3.11E−10	3.11E−10	Up	Chromosome 12 open reading frame 60
A_23_P161616	THC2024073	1.35635	5.76E−12	3.39E−10	3.39E−10	Up	FRA1_HUMAN (P15407) Fos-related antigen 1 (FRA-1), complete [THC2024073]
A_23_P123336	PPM2C	1.44116	6.53E−12	3.77E−10	3.77E−10	Up	Homo sapiens protein phosphatase 2C, magnesium-dependent, catalytic subunit (PPM2C), nuclear gene encoding mitochondrial protein, mRNA [NM_018444]
A_23_P338919	APEG1	2.206889	7.04E−12	4.04E−10	4.04E−10	Up	Homo sapiens aortic preferentially expressed protein 1 (APEG1), mRNA [NM_005876]
A_23_P36658	MGST1	1.605083	7.37E−12	4.2E−10	4.2E−10	Up	Homo sapiens microsomal glutathione S-transferase 1 (MGST1), transcript variant 1c, mRNA [NM_145791]
A_23_P102364	NGEF	3.066258	8.01E−12	4.54E−10	4.54E−10	Up	Homo sapiens neuronal guanine nucleotide exchange factor (NGEF), mRNA [NM_019850]
A_23_P159328	ANGPTL4	2.407577	8.2E−12	4.61E−10	4.61E−10	Up	Homo sapiens angiopoietin-like 4 (ANGPTL4), transcript variant 2, mRNA [NM_016109]
A_23_P206212	THBS1	1.585491	8.41E−12	4.71E−10	4.71E−10	Up	Homo sapiens thrombospondin 1 (THBS1), mRNA [NM_003246]
A_23_P349966	TMEM130	1.855769	8.65E−12	4.82E−10	4.82E−10	Up	Transmembrane protein 130
A_23_P91562	C21orf25	1.97297	9.76E−12	5.39E−10	5.39E−10	Up	Homo sapiens chromosome 21 open reading frame 25 (C21orf25), mRNA [NM_199050]
A_23_P388220	RALYL	1.413588	9.77E−12	5.39E−10	5.39E−10	Up	RALY RNA binding protein-like
A_23_P210274	PREI3	3.002367	1.08E−11	5.87E−10	5.87E−10	Up	Homo sapiens preimplantation protein 3 (PREI3), transcript variant 1, mRNA [NM_015387]
A_23_P314151	NOLC1	1.388253	1.09E−11	5.87E−10	5.87E−10	Up	Homo sapiens nucleolar and coiled-body phosphoprotein 1 (NOLC1), mRNA [NM_004741]
A_23_P131846	SNAI1	1.611608	1.1E−11	5.92E−10	5.92E−10	Up	Homo sapiens snail homolog 1 (Drosophila) (SNAI1), mRNA [NM_005985]
A_23_P63319	SOAT1	1.860516	1.13E−11	6.07E−10	6.07E−10	Up	Homo sapiens sterol *O*-acyltransferase (acyl-Coenzyme A: cholesterol acyltransferase) 1 (SOAT1), transcript variant 688113, mRNA [NM_003101]
A_23_P209360	KBTBD9	1.989405	1.23E−11	6.55E−10	6.55E−10	Up	Homo sapiens mRNA for KIAA1921 protein, partial cds. [AB067508]
A_23_P115726	SLC16A9	3.158842	1.38E−11	7.23E−10	7.23E−10	Up	Homo sapiens solute carrier family 16 (monocarboxylic acid transporters), member 9 (SLC16A9), mRNA [NM_194298]
A_23_P34478	GIPC2	1.365716	1.41E−11	7.35E−10	7.35E−10	Up	Homo sapiens PDZ domain protein GIPC2 (GIPC2), mRNA [NM_017655]
A_23_P404628	G1P2	2.306067	1.6E−11	8.25E−10	8.25E−10	Up	Homo sapiens interferon, alpha-inducible protein (clone IFI-15K) (G1P2), mRNA [NM_005101]
A_23_P89431	CCL2	3.259744	1.79E−11	9.12E−10	9.12E−10	Up	Homo sapiens chemokine (C–C motif) ligand 2 (CCL2), mRNA [NM_002982]
A_23_P69280	ALAS1	2.875007	1.85E−11	9.38E−10	9.38E−10	Up	Homo sapiens aminolevulinate, delta-, synthase 1 (ALAS1), transcript variant 1, mRNA [NM_000688]
A_23_P357780	FDX1	2.619767	2.15E−11	1.08E−09	1.08E−09	Up	Homo sapiens ferredoxin 1 (FDX1), nuclear gene encoding mitochondrial protein, mRNA [NM_004109]
A_23_P205336	C14orf129	1.997603	2.21E−11	1.11E−09	1.11E−09	Up	Homo sapiens cDNA FLJ20789 fis, clone COL01731. [AK000796]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P87889	DUSP16	1.391755	2.4E−11	1.19E−09	1.19E−09	Up	Homo sapiens mRNA for KIAA1700 protein, partial cds. [AB051487]
A_23_P342727	STARD13	1.564165	2.79E−11	1.37E−09	1.37E−09	Up	Homo sapiens START domain containing 13 (STARD13), transcript variant gamma, mRNA [NM_052851]
A_23_P361514	SNF1LK	1.719862	2.9E−11	1.41E−09	1.41E−09	Up	Homo sapiens mRNA for FLJ00263 protein. [AK131076]
A_23_P57836	#N/A	1.700577	2.91E−11	1.41E−09	1.41E−09	Up	Unknown
A_23_P152876	RAB34	1.984646	3.14E−11	1.49E−09	1.49E−09	Up	Homo sapiens RAB34, member RAS oncogene family (RAB34), mRNA [NM_031934]
A_23_P3532	LITAF	1.337206	3.38E−11	1.59E−09	1.59E−09	Up	Homo sapiens lipopolysaccharide-induced TNF factor (LITAF), mRNA [NM_004862]
A_23_P141636	DDX48	1.377814	3.47E−11	1.63E−09	1.63E−09	Up	Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 48 (DDX48), mRNA [NM_014740]
A_23_P207058	SOCS3	2.268049	3.72E−11	1.72E−09	1.72E−09	Up	Homo sapiens suppressor of cytokine signaling 3 (SOCS3), mRNA [NM_003955]
A_23_P166508	BC038245	1.630696	3.88E−11	1.8E−09	1.8E−09	Up	Homo sapiens, clone IMAGE:5241654, mRNA. [BC038245]
A_23_P73480	SGNE1	3.173007	4.01E−11	1.85E−09	1.85E−09	Up	Homo sapiens secretory granule, neuroendocrine protein 1 (7B2 protein) (SGNE1), mRNA [NM_003020]
A_23_P142560	ZFHX1B	1.510808	4.22E−11	1.94E−09	1.94E−09	Up	Homo sapiens zinc finger homeobox 1b (ZFHX1B), mRNA [NM_014795]
A_23_P62081	SGNE1	2.737254	4.68E−11	2.13E−09	2.13E−09	Up	Homo sapiens secretory granule, neuroendocrine protein 1 (7B2 protein) (SGNE1), mRNA [NM_003020]
A_23_P83220	HSPA5	1.379592	5.27E−11	2.37E−09	2.37E−09	Up	Homo sapiens heat shock 70 kDa protein 5 (glucose-regulated protein, 78 kDa) (HSPA5), mRNA [NM_005347]
A_23_P360232	MT1X	1.794576	5.48E−11	2.45E−09	2.45E−09	Up	Homo sapiens metallothionein 1X (MT1X), mRNA [NM_005952]
A_23_P208591	LDLR	1.966681	6.42E−11	2.82E−09	2.82E−09	Up	Homo sapiens low density lipoprotein receptor (familial hypercholesterolemia) (LDLR), mRNA [NM_000527]
A_23_P79398	IL1R2	2.283138	6.46E−11	2.83E−09	2.83E−09	Up	Homo sapiens interleukin 1 receptor, type II (IL1R2), transcript variant 1, mRNA [NM_004633]
A_23_P211039	ADAMTS1	2.04531	6.8E−11	2.94E−09	2.94E−09	Up	Homo sapiens a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 1 (ADAMTS1), mRNA [NM_006988]
A_23_P70670	CD83	1.865016	6.86E−11	2.96E−09	2.96E−09	Up	Homo sapiens CD83 antigen (activated B lymphocytes, immunoglobulin superfamily) (CD83), mRNA [NM_004233]
A_23_P411296	CEBPB	1.588112	7.01E−11	3E−09	3E−09	Up	Homo sapiens CCAAT/enhancer binding protein (C/EBP), beta (CEBPB), mRNA [NM_005194]
A_23_P126925	SFPQ	1.349485	7.75E−11	3.24E−09	3.24E−09	Up	Homo sapiens splicing factor proline/glutamine rich (polypyrimidine tract binding protein associated) (SFPQ), mRNA [NM_005066]
A_23_P56956	TXNDC7	1.613258	8.15E−11	3.38E−09	3.38E−09	Up	Homo sapiens thioredoxin domain containing 7 (protein disulfideisomerase) (TXNDC7), mRNA [NM_005742]
A_23_P15179	MT1F	1.836252	8.63E−11	3.55E−09	3.55E−09	Up	Homo sapiens metallothionein 1F (functional) (MT1F), mRNA [NM_005949]
A_23_P357724	KCNK3	2.106029	9.52E−11	3.88E−09	3.88E−09	Up	Homo sapiens potassium channel, subfamily K, member 3 (KCNK3), mRNA [NM_002246]
A_23_P354704	ST8SIA1	1.408187	1.13E−10	4.54E−09	4.54E−09	Up	Homo sapiens sialyltransferase 8A (alpha-N-acetylneuraminate: alpha-2,8-sialyltransferase, GD3 synthase) (SIAT8A), mRNA [NM_003034]
A_23_P144188	SLC33A1	1.382647	1.39E−10	5.45E−09	5.45E−09	Up	Homo sapiens solute carrier family 33 (acetyl-CoA transporter), member 1 (SLC33A1), mRNA [NM_004733]
A_23_P378430	STARD6	3.457445	1.42E−10	5.55E−09	5.55E−09	Up	Homo sapiens START domain containing 6 (STARD6), mRNA [NM_139171]
A_23_P429977	KCNQ1	2.515565	1.54E−10	5.95E−09	5.95E−09	Up	Homo sapiens potassium voltage-gated channel, KQT-like subfamily, member 1 (KCNQ1), transcript variant 1, mRNA [NM_000218]
A_23_P256470	NPY	2.429566	1.67E−10	6.38E−09	6.38E−09	Up	Homo sapiens neuropeptide Y (NPY), mRNA [NM_000905]
A_23_P54840	MT1A	1.518918	1.91E−10	7.28E−09	7.28E−09	Up	Homo sapiens metallothionein 1A (functional) (MT1A), mRNA [NM_005946]
A_23_P132121	SNF1LK	1.368712	2.31E−10	8.61E−09	8.61E−09	Up	Homo sapiens SNF1-like kinase (SNF1LK), mRNA [NM_173354]
A_23_P150016	DUSP5	1.433934	2.65E−10	9.69E−09	9.69E−09	Up	Homo sapiens dual specificity phosphatase 5 (DUSP5), mRNA [NM_004419]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P134125	MAP3K5	1.614955	2.81E−10	1.03E−08	1.03E−08	Up	Homo sapiens mitogen-activated protein kinase kinasekinase 5 (MAP3K5), mRNA [NM_005923]
A_23_P257478	CYP21A2	2.19999	2.92E−10	1.06E−08	1.06E−08	Up	Homo sapiens cytochrome P450, family 21, subfamily A, polypeptide 2 (CYP21A2), mRNA [NM_000500]
A_23_P162616	MGC35366	3.111246	3.34E−10	1.19E−08	1.19E−08	Up	Homo sapiens hypothetical protein MGC35366 (MGC35366), mRNA [NM_152435]
A_23_P375906	MAPK4	1.787338	4.02E−10	1.4E−08	1.4E−08	Up	Homo sapiens mitogen-activated protein kinase 4 (MAPK4), mRNA [NM_002747]
A_23_P216167	PSD3	2.098887	4.05E−10	1.41E−08	1.41E−08	Up	Homo sapiens pleckstrin and Sec7 domain containing 3 (PSD3), transcript variant 1, mRNA [NM_015310]
A_23_P214108	TPMT	1.610475	4.8E−10	1.65E−08	1.65E−08	Up	Homo sapiens thiopurine S-methyltransferase (TPMT), mRNA [NM_000367]
A_23_P378416	GPM6B	1.923834	5.85E−10	1.96E−08	1.96E−08	Up	Homo sapiens glycoprotein M6B (GPM6B), transcript variant 3, mRNA [NM_005278]
A_23_P154037	AOX1	2.306045	6.16E−10	2.05E−08	2.05E−08	Up	Homo sapiens aldehyde oxidase 1 (AOX1), mRNA [NM_001159]
A_23_P155596	FMO3	2.047263	6.94E−10	2.28E−08	2.28E−08	Up	Homo sapiens flavin-containing monooxygenase 3 (FMO3), transcript variant 1, mRNA [NM_006894]
A_23_P138168	CNN3	1.371512	6.99E−10	2.29E−08	2.29E−08	Up	Homo sapiens calponin 3, acidic (CNN3), mRNA [NM_001839]
A_23_P216335	THC2050017	1.359185	7.5E−10	2.43E−08	2.43E−08	Up	Q9SS92 (Q9SS92) F4P13.17 protein, partial (3%) [THC2050017]
A_23_P75358	CTSD	1.337872	7.96E−10	2.56E−08	2.56E−08	Up	Homo sapiens cDNA FLJ12231 fis, clone MAMMA1001191. [AK022293]
A_23_P106611	WFDC1	1.643367	8.91E−10	2.8E−08	2.8E−08	Up	Homo sapiens WAP four-disulfide core domain 1 (WFDC1), mRNA [NM_021197]
A_23_P120644	HIGD1AP16	1.49479	9.06E−10	2.84E−08	2.84E−08	Up	HIG1 hypoxia-inducible domain family member 1A pseudogene 16
A_23_P6344	SDF2L1	1.421476	9.38E−10	2.92E−08	2.92E−08	Up	Homo sapiens stromal cell-derived factor 2-like 1 (SDF2L1), mRNA [NM_022044]
A_23_P163782	MT1H	1.761943	1.01E−09	3.09E−08	3.09E−08	Up	Homo sapiens metallothionein 1H (MT1H), mRNA [NM_005951]
A_23_P300033	PDGFRA	2.505707	1.11E−09	3.35E−08	3.35E−08	Up	Homo sapiens platelet-derived growth factor receptor, alpha polypeptide (PDGFRA), mRNA [NM_006206]
A_23_P21485	PID1	1.595616	1.11E−09	3.35E−08	3.35E−08	Up	Phosphotyrosine interaction domain containing 1
A_23_P129695	VASN	2.204315	1.12E−09	3.37E−08	3.37E−08	Up	vasorin
A_23_P203115	TMEM25	1.572761	1.18E−09	3.52E−08	3.52E−08	Up	Homo sapiens transmembrane protein 25 (TMEM25), mRNA [NM_032780]
A_23_P142849	RND3	2.022994	1.21E−09	3.61E−08	3.61E−08	Up	Homo sapiens Rho family GTPase 3 (RND3), mRNA [NM_005168]
A_23_P42575	CALD1	1.437294	1.23E−09	3.66E−08	3.66E−08	Up	Homo sapiens caldesmon 1 (CALD1), transcript variant 4, mRNA [NM_033139]
A_23_P107356	NALP1	2.039984	1.26E−09	3.72E−08	3.72E−08	Up	Homo sapiens NACHT, leucine-rich repeat and PYD (pyrin domain) containing 1, mRNA (cDNA clone MGC:57544 IMAGE:5756099), complete cds. [BC051787]
A_23_P303242	MT1X	1.828041	1.26E−09	3.74E−08	3.74E−08	Up	Homo sapiens metallothionein 1X (MT1X), mRNA [NM_005952]
A_23_P414343	MT1J	1.660521	1.47E−09	4.26E−08	4.26E−08	Up	Homo sapiens metallothionein 1J (MT1J), mRNA [NM_175622]
A_23_P8754	AASS	1.342999	1.48E−09	4.28E−08	4.28E−08	Up	Homo sapiens aminoadipate-semialdehyde synthase (AASS), mRNA [NM_005763]
A_23_P208101	MAPK4	2.977019	1.51E−09	4.36E−08	4.36E−08	Up	Mitogen-activated protein kinase 4 (EC 2.7.1.37) (Extracellular signal-regulated kinase 4) (ERK-4) (MAP kinase isoform p63) (p63- MAPK). [Source:Uniprot/SWISSPROT;Acc:P31152] [ENST00000269463]
A_23_P40885	HIG1	1.494517	1.65E−09	4.7E−08	4.7E−08	Up	Homo sapiens likely ortholog of mouse hypoxia induced gene 1 (HIG1), mRNA [NM_014056]
A_23_P81770	PTP4A1	2.460092	1.72E−09	4.87E−08	4.87E−08	Up	Homo sapiens protein tyrosine phosphatase type IVA, member 1 (PTP4A1), mRNA [NM_003463]
A_23_P56197	CRLF1	2.121983	2.26E−09	6.22E−08	6.22E−08	Up	Homo sapiens cytokine receptor-like factor 1 (CRLF1), mRNA [NM_004750]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P391906	KIAA1913	1.865772	2.38E−09	6.49E−08	6.49E−08	Up	Homo sapiens KIAA1913, mRNA (cDNA clone MGC:50847 IMAGE:5760073), complete cds. [BC044246]
A_23_P3261	PDE8A	1.549695	2.57E−09	6.91E−08	6.91E−08	Up	Homo sapiens phosphodiesterase 8A (PDE8A), transcript variant 5, mRNA [NM_173457]
A_23_P26037	FRMD5	1.961081	2.62E−09	7.02E−08	7.02E−08	Up	FERM domain containing 5
A_23_P4821	JUNB	1.357455	3.31E−09	8.61E−08	8.61E−08	Up	Homo sapiens jun B proto-oncogene (JUNB), mRNA [NM_002229]
A_23_P156708	TNXB	2.221748	3.54E−09	9.17E−08	9.17E−08	Up	Homo sapiens tenascin XB (TNXB), transcript variant XB, mRNA [NM_019105]
A_23_P126706	ANGPTL1	1.974309	3.55E−09	9.19E−08	9.19E−08	Up	Homo sapiens angiopoietin-like 1 (ANGPTL1), mRNA [NM_004673]
A_23_P121795	ARGBP2	2.099097	3.63E−09	9.35E−08	9.35E−08	Up	Homo sapiens Arg/Abl-interacting protein ArgBP2 (ARGBP2), transcript variant 2, mRNA [NM_021069]
A_23_P98375	FDX1	2.511754	3.75E−09	9.67E−08	9.67E−08	Up	Homo sapiens ferredoxin 1 (FDX1), nuclear gene encoding mitochondrial protein, mRNA [NM_004109]
A_23_P94333	ENPP2	1.509263	3.84E−09	9.84E−08	9.84E−08	Up	Homo sapiens ectonucleotidepyrophosphatase/phosphodiesterase 2 (autotaxin) (ENPP2), mRNA [NM_006209]
A_23_P20573	THC2084558	3.544464	3.93E−09	1E−07	1E−07	Up	BC029647 RUSC2 protein {Homo sapiens;}, partial (40%) [THC2084558]
A_23_P14621	FGF7	1.736063	4.4E−09	1.11E−07	1.11E−07	Up	Homo sapiens fibroblast growth factor 7 (keratinocyte growth factor) (FGF7), mRNA [NM_002009]
A_23_P379481	DHCR24	1.656798	4.41E−09	1.11E−07	1.11E−07	Up	Homo sapiens 24-dehydrocholesterol reductase (DHCR24), mRNA [NM_014762]
A_23_P50946	RAMP1	1.6298	4.95E−09	1.23E−07	1.23E−07	Up	Homo sapiens receptor (calcitonin) activity modifying protein 1 (RAMP1), mRNA [NM_005855]
A_23_P38732	CDH2	2.017234	4.99E−09	1.24E−07	1.24E−07	Up	Homo sapiens cadherin 2, type 1, *N*-cadherin (neuronal) (CDH2), mRNA [NM_001792]
A_23_P167920	DLL1	1.354522	5.15E−09	1.27E−07	1.27E−07	Up	Homo sapiens delta-like 1 (Drosophila) (DLL1), mRNA [NM_005618]
A_23_P38735	CDH19	2.245546	5.27E−09	1.3E−07	1.3E−07	Up	Homo sapiens cadherin 19, type 2 (CDH19), mRNA [NM_021153]
A_23_P348737	NR2F1	1.883752	5.4E−09	1.33E−07	1.33E−07	Up	Homo sapiens nuclear receptor subfamily 2, group F, member 1 (NR2F1), mRNA [NM_005654]
A_23_P151506	PLEK2	1.425105	5.46E−09	1.34E−07	1.34E−07	Up	Homo sapiens pleckstrin 2 (PLEK2), mRNA [NM_016445]
A_23_P162047	DKK3	1.802346	5.54E−09	1.36E−07	1.36E−07	Up	Homo sapiens dickkopf homolog 3 (Xenopuslaevis) (DKK3), mRNA [NM_013253]
A_23_P56630	STAT1	1.734679	5.93E−09	1.45E−07	1.45E−07	Up	Homo sapiens signal transducer and activator of transcription 1, 91 kDa (STAT1), transcript variant alpha, mRNA [NM_007315]
A_23_P161647	PC	1.526131	6.67E−09	1.59E−07	1.59E−07	Up	Homo sapiens pyruvate carboxylase (PC), nuclear gene encoding mitochondrial protein, transcript variant A, mRNA [NM_000920]
A_23_P32253	NFIL3	1.890335	7.12E−09	1.68E−07	1.68E−07	Up	Homo sapiens nuclear factor, interleukin 3 regulated (NFIL3), mRNA [NM_005384]
A_23_P6674	LXN	1.80166	7.33E−09	1.73E−07	1.73E−07	Up	Homo sapiens latexin (LXN), mRNA [NM_020169]
A_23_P65278	NBEA	1.353914	7.61E−09	1.79E−07	1.79E−07	Up	Homo sapiens neurobeachin (NBEA), mRNA [NM_015678]
A_23_P169189	IKBKAP	1.420272	8.03E−09	1.87E−07	1.87E−07	Up	Homo sapiens inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein (IKBKAP), mRNA [NM_003640]
A_23_P416581	GNAZ	1.948799	9.12E−09	2.06E−07	2.06E−07	Up	Homo sapiens guanine nucleotide binding protein (G protein), alpha z polypeptide (GNAZ), mRNA [NM_002073]
A_23_P111689	THC2124728	1.666303	9.76E−09	2.19E−07	2.19E−07	Up	PBEF_HUMAN (P43490) Pre-B cell enhancing factor precursor, partial (16%) [THC2124728]
A_23_P75111	CYP17A1	2.459744	9.99E−09	2.22E−07	2.22E−07	Up	Homo sapiens cytochrome P450, family 17, subfamily A, polypeptide 1 (CYP17A1), mRNA [NM_000102]
A_23_P374862	DAF	1.337354	1.02E−08	2.26E−07	2.26E−07	Up	Homo sapiens decay accelerating factor for complement (CD55, Cromer blood group system) (DAF), mRNA [NM_000574]
A_23_P24903	P2RY2	1.627155	1.03E−08	2.28E−07	2.28E−07	Up	Homo sapiens purinergic receptor P2Y, G protein-coupled, 2 (P2RY2), transcript variant 1, mRNA [NM_176072]
A_23_P25964	GALC	1.508007	1.04E−08	2.31E−07	2.31E−07	Up	Homo sapiens galactosylceramidase (Krabbe disease) (GALC), mRNA [NM_000153]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P144369	NAP1L5	2.076834	1.36E−08	2.92E−07	2.92E−07	Up	Homo sapiens nucleosome assembly protein 1-like 5 (NAP1L5), mRNA [NM_153757]
A_23_P97265	GPATC4	1.398574	1.39E−08	2.98E−07	2.98E−07	Up	Homo sapiens G patch domain containing 4 (GPATC4), transcript variant 1, mRNA [NM_015590]
A_23_P164654	APOE	2.317898	1.52E−08	3.22E−07	3.22E−07	Up	Homo sapiens apolipoprotein E (APOE), mRNA [NM_000041]
A_23_P305060	PBEF1	2.273275	1.58E−08	3.31E−07	3.31E−07	Up	Homo sapiens pre-B-cell colony enhancing factor 1 (PBEF1), transcript variant 1, mRNA [NM_005746]
A_23_P94319	KIAA0711	1.727265	1.59E−08	3.33E−07	3.33E−07	Up	Homo sapiens KIAA0711 gene product (KIAA0711), mRNA [NM_014867]
A_23_P7451	AF087978	2.034459	1.63E−08	3.4E−07	3.4E−07	Up	Homo sapiens full-length insert cDNA clone YW26E10. [AF087978]
A_23_P123234	#N/A	1.3744	1.7E−08	3.54E−07	3.54E−07	Up	Unknown
A_23_P127948	ADM	2.000368	1.8E−08	3.73E−07	3.73E−07	Up	Homo sapiens adrenomedullin (ADM), mRNA [NM_001124]
A_23_P153320	ICAM1	1.374833	1.92E−08	3.95E−07	3.95E−07	Up	Homo sapiens intercellular adhesion molecule 1 (CD54), human rhinovirus receptor (ICAM1), mRNA [NM_000201]
A_23_P12884	GRK5	1.612415	2.36E−08	4.69E−07	4.69E−07	Up	Homo sapiens G protein-coupled receptor kinase 5 (GRK5), mRNA [NM_005308]
A_23_P108574	PRKD3	1.728524	2.62E−08	5.14E−07	5.14E−07	Up	Homo sapiens protein kinase D3 (PRKD3), mRNA [NM_005813]
A_23_P119562	DF	2.116595	2.86E−08	5.56E−07	5.56E−07	Up	Homo sapiens D component of complement (adipsin) (DF), mRNA [NM_001928]
A_23_P60933	MT1G	1.80628	3.61E−08	6.83E−07	6.83E−07	Up	Homo sapiens metallothionein 1G (MT1G), mRNA [NM_005950]
A_23_P120845	XBP1	1.504217	3.93E−08	7.31E−07	7.31E−07	Up	Homo sapiens X-box binding protein 1 (XBP1), mRNA [NM_005080]
A_23_P31810	CEBPD	1.512557	4.54E−08	8.35E−07	8.35E−07	Up	Homo sapiens CCAAT/enhancer binding protein (C/EBP), delta (CEBPD), mRNA [NM_005195]
A_23_P91802	ECGF1	1.445231	4.58E−08	8.38E−07	8.38E−07	Up	Homo sapiens endothelial cell growth factor 1 (platelet-derived) (ECGF1), mRNA [NM_001953]
A_23_P82245	ENST00000328742	1.715801	4.95E−08	8.98E−07	8.98E−07	Up	Unknown
A_23_P143143	ID2	1.543481	5.7E−08	1.02E−06	1.02E−06	Up	Homo sapiens inhibitor of DNA binding 2, dominant negative helix-loop-helix protein (ID2), mRNA [NM_002166]
A_23_P82868	PLAT	2.031262	6.26E−08	1.1E−06	1.1E−06	Up	Homo sapiens plasminogen activator, tissue (PLAT), transcript variant 1, mRNA [NM_000930]
A_23_P12643	AS3MT	2.569142	6.42E−08	1.13E−06	1.13E−06	Up	Homo sapiens arsenic (+3 oxidation state) methyltransferase (AS3MT), mRNA [NM_020682]
A_23_P5365	RPRM	2.393004	6.72E−08	1.18E−06	1.18E−06	Up	Homo sapiens reprimo, TP53 dependant G2 arrest mediator candidate (RPRM), mRNA [NM_019845]
A_23_P26965	CCL13	1.754046	6.9E−08	1.2E−06	1.2E−06	Up	Homo sapiens chemokine (C–C motif) ligand 13 (CCL13), mRNA [NM_005408]
A_23_P132956	UCHL1	2.23684	6.9E−08	1.2E−06	1.2E−06	Up	Homo sapiens ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase) (UCHL1), mRNA [NM_004181]
A_23_P151805	FBLN5	1.487334	7.21E−08	1.25E−06	1.25E−06	Up	Homo sapiens fibulin 5 (FBLN5), mRNA [NM_006329]
A_23_P103951	#N/A	1.404991	7.62E−08	1.3E−06	1.3E−06	Up	Unknown
A_23_P257087	PDK4	1.589706	7.86E−08	1.34E−06	1.34E−06	Up	Homo sapiens pyruvate dehydrogenase kinase, isoenzyme 4 (PDK4), mRNA [NM_002612]
A_23_P128230	NR4A1	1.853378	9.07E−08	1.51E−06	1.51E−06	Up	Homo sapiens nuclear receptor subfamily 4, group A, member 1 (NR4A1), transcript variant 1, mRNA [NM_002135]
A_23_P65558	MGAT2	1.635583	9.13E−08	1.52E−06	1.52E−06	Up	Homo sapiens mannosyl (alpha-1,6-)-glycoprotein beta-1,2-*N*-acetylglucosaminyltransferase (MGAT2), mRNA [NM_002408]
A_23_P37983	MT1B	1.841945	9.28E−08	1.54E−06	1.54E−06	Up	Homo sapiens metallothionein 1B (functional) (MT1B), mRNA [NM_005947]
A_23_P258190	AKR1B1	1.840337	9.58E−08	1.58E−06	1.58E−06	Up	Homo sapiens aldo-ketoreductase family 1, member B1 (aldose reductase) (AKR1B1), mRNA [NM_001628]
A_23_P213184	ADH1B	2.386573	9.7E−08	1.6E−06	1.6E−06	Up	Homo sapiens alcohol dehydrogenase IB (class I), beta polypeptide (ADH1B), mRNA [NM_000668]
A_23_P2831	EDNRB	1.448551	9.72E−08	1.6E−06	1.6E−06	Up	Homo sapiens endothelin receptor type B (EDNRB), transcript variant 2, mRNA [NM_003991]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P16915	QPCT	2.371931	1.03E−07	1.68E−06	1.68E−06	Up	Homo sapiens glutaminyl-peptide cyclotransferase (glutaminylcyclase) (QPCT), mRNA [NM_012413]
A_23_P146274	STMN2	2.180835	1.25E−07	2.01E−06	2.01E−06	Up	Homo sapiens stathmin-like 2 (STMN2), mRNA [NM_007029]
A_23_P363936	HSPA4L	1.528526	1.52E−07	2.39E−06	2.39E−06	Up	Homo sapiens heat shock 70 kDa protein 4-like (HSPA4L), mRNA [NM_014278]
A_23_P102331	SCN7A	1.350016	1.53E−07	2.4E−06	2.4E−06	Up	Q16278 (Q16278) Voltage-dependent sodium channel alpha subunit protein (Fragment), partial (18%) [THC2123516]
A_23_P33723	CD163	1.510097	1.78E−07	2.72E−06	2.72E−06	Up	Homo sapiens CD163 antigen (CD163), transcript variant 1, mRNA [NM_004244]
A_23_P206701	MT1G	1.98697	1.81E−07	2.77E−06	2.77E−06	Up	Homo sapiens metallothionein 1G (MT1G), mRNA [NM_005950]
A_23_P144274	MARLIN1	1.663905	1.84E−07	2.8E−06	2.8E−06	Up	Homo sapiens multiple coiled-coil GABABR1-binding protein (MARLIN1), mRNA [NM_144720]
A_23_P13609	PBP	1.421202	1.85E−07	2.82E−06	2.82E−06	Up	Homo sapiens prostatic binding protein (PBP), mRNA [NM_002567]
A_23_P86470	CH25H	1.57869	1.86E−07	2.83E−06	2.83E−06	Up	Homo sapiens cholesterol 25-hydroxylase (CH25H), mRNA [NM_003956]
A_23_P70968	HOXA7	1.380763	1.92E−07	2.9E−06	2.9E−06	Up	Homo sapiens homeo box A7 (HOXA7), mRNA [NM_006896]
A_23_P82526	ABCB1	2.895077	1.96E−07	2.96E−06	2.96E−06	Up	Homo sapiens ATP-binding cassette, subfamily B (MDR/TAP), member 1 (ABCB1), mRNA [NM_000927]
A_23_P165418	BZW1	1.554534	2.1E−07	3.14E−06	3.14E−06	Up	Homo sapiens basic leucine zipper and W2 domains 1 (BZW1), mRNA [NM_014670]
A_23_P18078	RARRES1	2.610513	2.22E−07	3.3E−06	3.3E−06	Up	Homo sapiens retinoic acid receptor responder (tazarotene induced) 1 (RARRES1), transcript variant 2, mRNA [NM_002888]
A_23_P71290	YWHAZ	1.364631	2.4E−07	3.52E−06	3.52E−06	Up	Homo sapiens tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide (YWHAZ), transcript variant 2, mRNA [NM_145690]
A_23_P259442	CPE	1.760612	2.42E−07	3.55E−06	3.55E−06	Up	Homo sapiens carboxypeptidase E (CPE), mRNA [NM_001873]
A_23_P83098	ALDH1A1	1.846995	2.73E−07	3.94E−06	3.94E−06	Up	Homo sapiens aldehyde dehydrogenase 1 family, member A1 (ALDH1A1), mRNA [NM_000689]
A_23_P434809	S100A8	2.594844	2.92E−07	4.18E−06	4.18E−06	Up	Homo sapiens S100 calcium binding protein A8 (calgranulin A) (S100A8), mRNA [NM_002964]
A_23_P82121	ARHGAP18	1.364924	3.25E−07	4.59E−06	4.59E−06	Up	Homo sapiens Rho GTPase activating protein 18 (ARHGAP18), mRNA [NM_033515]
A_23_P37484	CHSY1	1.65727	3.32E−07	4.67E−06	4.67E−06	Up	Homo sapiens carbohydrate (chondroitin) synthase 1 (CHSY1), mRNA [NM_014918]
A_23_P154806	EPB41L1	1.413839	3.48E−07	4.86E−06	4.86E−06	Up	Homo sapiens erythrocyte membrane protein band 4.1-like 1 (EPB41L1), transcript variant 1, mRNA [NM_012156]
A_23_P47725	MAP6	1.434058	4.09E−07	5.58E−06	5.58E−06	Up	Homo sapiens microtubule-associated protein 6 (MAP6), transcript variant 1, mRNA [NM_033063]
A_23_P149322	LOC55924	1.516291	4.11E−07	5.6E−06	5.6E−06	Up	Homo sapiens hypothetical protein LOC55924 (LOC55924), transcript variant 1, mRNA [NM_019099]
A_23_P200288	S100A8	2.275684	4.22E−07	5.72E−06	5.72E−06	Up	Homo sapiens S100 calcium binding protein A8 (calgranulin A) (S100A8), mRNA [NM_002964]
A_23_P105803	FGF9	1.651103	4.42E−07	5.95E−06	5.95E−06	Up	Homo sapiens fibroblast growth factor 9 (glia-activating factor) (FGF9), mRNA [NM_002010]
A_23_P112281	TMOD1	1.396958	4.46E−07	5.99E−06	5.99E−06	Up	Homo sapiens tropomodulin 1 (TMOD1), mRNA [NM_003275]
A_23_P259156	RGN	1.717432	4.65E−07	6.22E−06	6.22E−06	Up	Homo sapiens regucalcin (senescence marker protein-30) (RGN), transcript variant 1, mRNA [NM_004683]
A_23_P72968	ARHGAP36	3.028372	5.03E−07	6.65E−06	6.65E−06	Up	Rho GTPase activating protein 36
A_23_P71037	IL6	1.851961	5.17E−07	6.8E−06	6.8E−06	Up	Homo sapiens interleukin 6 (interferon, beta 2) (IL6), mRNA [NM_000600]
A_23_P211727	FGF12	2.169796	5.21E−07	6.84E−06	6.84E−06	Up	Homo sapiens fibroblast growth factor 12 (FGF12), transcript variant 2, mRNA [NM_004113]
A_23_P93591	GJA1	1.425888	5.31E−07	6.95E−06	6.95E−06	Up	Homo sapiens gap junction protein, alpha 1, 43 kDa (connexin 43) (GJA1), mRNA [NM_000165]
A_23_P42414	NEDD9	1.564625	6.92E−07	8.75E−06	8.75E−06	Up	Homo sapiens neural precursor cell expressed, developmentally down-regulated 9 (NEDD9), mRNA [NM_006403]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P111402	THSD2	1.902868	6.95E−07	8.79E−06	8.79E−06	Up	Homo sapiens thrombospondin, type I, domain containing 2 (THSD2), mRNA [NM_032784]
A_23_P81158	ADH1C	1.978076	7.04E−07	8.88E−06	8.88E−06	Up	Homo sapiens alcohol dehydrogenase 1C (class I), gamma polypeptide (ADH1C), mRNA [NM_000669]
A_23_P124598	SLCO2A1	1.406679	9.47E−07	1.15E−05	1.15E−05	Up	Homo sapiens solute carrier organic anion transporter family, member 2A1 (SLCO2A1), mRNA [NM_005630]
A_23_P503182	ABR	1.563686	9.91E−07	1.19E−05	1.19E−05	Up	Homo sapiens active BCR-related gene (ABR), transcript variant 1, mRNA [NM_021962]
A_23_P211631	FBLN1	1.994065	1.04E−06	1.24E−05	1.24E−05	Up	Homo sapiens fibulin 1 (FBLN1), transcript variant D, mRNA [NM_006486]
A_23_P161559	RAB38	1.565142	1.06E−06	1.27E−05	1.27E−05	Up	Homo sapiens RAB38, member RAS oncogene family (RAB38), mRNA [NM_022337]
A_23_P87013	TAGLN	1.433193	1.09E−06	1.3E−05	1.3E−05	Up	Homo sapiens transgelin (TAGLN), transcript variant 2, mRNA [NM_003186]
A_23_P52336	UNC5B	1.401067	1.1E−06	1.31E−05	1.31E−05	Up	Homo sapiens unc-5 homolog B (C. elegans) (UNC5B), mRNA [NM_170744]
A_23_P203558	HBB	2.326188	1.12E−06	1.33E−05	1.33E−05	Up	Homo sapiens hemoglobin, beta (HBB), mRNA [NM_000518]
A_23_P64873	DCN	2.359446	1.31E−06	1.51E−05	1.51E−05	Up	Homo sapiens decorin (DCN), transcript variant A1, mRNA [NM_001920]
A_23_P6321	CLDN5	1.370715	1.6E−06	1.79E−05	1.79E−05	Up	Homo sapiens claudin 5 (transmembrane protein deleted in velocardiofacial syndrome) (CLDN5), mRNA [NM_003277]
A_23_P111132	HSPA1A	1.716585	1.64E−06	1.83E−05	1.83E−05	Up	Homo sapiens heat shock 70 kDa protein 1A (HSPA1A), mRNA [NM_005345]
A_23_P500998	HOXA9	1.433317	1.8E−06	1.98E−05	1.98E−05	Up	Homo sapiens homeo box A9 (HOXA9), transcript variant 1, mRNA [NM_152739]
A_23_P4649	APOC1	2.143801	1.92E−06	2.09E−05	2.09E−05	Up	Homo sapiens apolipoprotein C-I (APOC1), mRNA [NM_001645]
A_23_P417974	AQP11	1.78482	1.94E−06	2.11E−05	2.11E−05	Up	Homo sapiens aquaporin 11 (AQP11), mRNA [NM_173039]
A_23_P304450	GATA6	1.668494	2.13E−06	2.28E−05	2.28E−05	Up	Homo sapiens GATA binding protein 6 (GATA6), mRNA [NM_005257]
A_23_P17998	HES1	1.363344	2.14E−06	2.28E−05	2.28E−05	Up	Homo sapiens hairy and enhancer of split 1, (Drosophila) (HES1), mRNA [NM_005524]
A_23_P103996	GCLM	2.083887	2.41E−06	2.53E−05	2.53E−05	Up	Homo sapiens glutamate-cysteine ligase, modifier subunit (GCLM), mRNA [NM_002061]
A_23_P206724	MT1E	1.80627	2.64E−06	2.76E−05	2.76E−05	Up	Homo sapiens metallothionein 1E (functional) (MT1E), mRNA [NM_175617]
A_23_P99515	MEDAG	1.409506	3.19E−06	3.23E−05	3.23E−05	Up	mesenteric estrogen dependent adipogenesis
A_23_P60776	PSPHL	3.127369	3.2E−06	3.23E−05	3.23E−05	Up	Homo sapiens phosphoserine phosphatase-like, mRNA (cDNA clone IMAGE:5552627), partial cds. [BC065228]
A_23_P202448	CXCL12	1.899738	3.44E−06	3.44E−05	3.44E−05	Up	Homo sapiens chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) (CXCL12), mRNA [NM_199168]
A_23_P347632	MTSS1	1.358882	3.45E−06	3.45E−05	3.45E−05	Up	Homo sapiens metastasis suppressor 1 (MTSS1), mRNA [NM_014751]
A_23_P45536	MCF2	1.446303	3.76E−06	3.73E−05	3.73E−05	Up	Homo sapiens MCF.2 cell line derived transforming sequence (MCF2), mRNA [NM_005369]
A_23_P160286	PRG4	2.377518	3.95E−06	3.88E−05	3.88E−05	Up	Homo sapiens proteoglycan 4 (PRG4), mRNA [NM_005807]
A_23_P143845	TIPARP	1.371417	4.31E−06	4.19E−05	4.19E−05	Up	Homo sapiens TCDD-inducible poly(ADP-ribose) polymerase (TIPARP), mRNA [NM_015508]
A_23_P258132	DKFZp564I1922	1.617696	5.1E−06	4.86E−05	4.86E−05	Up	Homo sapiens adlican (DKFZp564I1922), mRNA [NM_015419]
A_23_P205959	ALDH1A3	1.421167	5.67E−06	5.31E−05	5.31E−05	Up	Homo sapiens aldehyde dehydrogenase 1 family, member A3 (ALDH1A3), mRNA [NM_000693]
A_23_P58359	ADH1A	1.532461	5.74E−06	5.37E−05	5.37E−05	Up	Homo sapiens alcohol dehydrogenase 1A (class I), alpha polypeptide (ADH1A), mRNA [NM_000667]
A_23_P164170	PRKAR1A	1.386706	5.82E−06	5.43E−05	5.43E−05	Up	Homo sapiens protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1) (PRKAR1A), transcript variant 1, mRNA [NM_002734]
A_23_P426305	AOC3	1.779258	6.3E−06	5.82E−05	5.82E−05	Up	Homo sapiens amine oxidase, copper containing 3 (vascular adhesion protein 1) (AOC3), mRNA [NM_003734]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P163306	CGNL1	1.416971	7.15E−06	6.51E−05	6.51E−05	Up	Homo sapiens cingulin-like 1 (CGNL1), mRNA [NM_032866]
A_23_P74609	G0S2	1.541931	7.19E−06	6.54E−05	6.54E−05	Up	Homo sapiens putative lymphocyte G0/G1 switch gene (G0S2), mRNA [NM_015714]
A_23_P139114	SERPING1	1.444638	7.31E−06	6.61E−05	6.61E−05	Up	Homo sapiens serine (or cysteine) proteinase inhibitor, clade G (C1 inhibitor), member 1, (angioedema, hereditary) (SERPING1), mRNA [NM_000062]
A_23_P257043	GEM	1.55488	8.51E−06	7.53E−05	7.53E−05	Up	Homo sapiens GTP binding protein overexpressed in skeletal muscle (GEM), transcript variant 1, mRNA [NM_005261]
A_23_P146134	MGC1136	1.499155	9.78E−06	8.46E−05	8.46E−05	Up	Homo sapiens hypothetical protein MGC1136 (MGC1136), mRNA [NM_024025]
A_23_P48513	IFI27	1.476551	1.17E−05	9.88E−05	9.88E−05	Up	Homo sapiens interferon, alpha-inducible protein 27 (IFI27), transcript variant a, mRNA [NM_005532]
A_23_P60802	ADRA2C	1.517617	1.47E−05	0.000121	0.000121	Up	Homo sapiens adrenergic, alpha-2C-, receptor (ADRA2C), mRNA [NM_000683]
A_23_P212905	CXCL1	1.650066	1.58E−05	0.000129	0.000129	Up	Homo sapiens chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha) (CXCL1), mRNA [NM_001511]
A_23_P82929	NOV	2.611517	1.58E−05	0.000129	0.000129	Up	Homo sapiens nephroblastoma overexpressed gene (NOV), mRNA [NM_002514]
A_23_P400449	KIAA1576	1.785386	1.73E−05	0.000139	0.000139	Up	Homo sapiens KIAA1576 protein (KIAA1576), mRNA [NM_020927]
A_23_P257231	AGXT2L1	1.668258	1.78E−05	0.000142	0.000142	Up	Homo sapiens alanine-glyoxylate aminotransferase 2-like 1 (AGXT2L1), mRNA [NM_031279]
A_23_P254102	PI16	1.772525	1.99E−05	0.000156	0.000156	Up	Homo sapiens protease inhibitor 16 (PI16), mRNA [NM_153370]
A_23_P7752	SEMA6A	1.499301	2.05E−05	0.000161	0.000161	Up	Homo sapiens sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6A (SEMA6A), mRNA [NM_020796]
A_23_P35995	ASAM	1.354771	2.12E−05	0.000165	0.000165	Up	Homo sapiens adipocyte-specific adhesion molecule (ASAM), mRNA [NM_024769]
A_23_P114883	FMOD	1.753993	2.14E−05	0.000166	0.000166	Up	Homo sapiens fibromodulin (FMOD), mRNA [NM_002023]
A_23_P125233	CNN1	1.531608	2.22E−05	0.000171	0.000171	Up	Homo sapiens calponin 1, basic, smooth muscle (CNN1), mRNA [NM_001299]
A_23_P362148	DNER	1.635414	2.27E−05	0.000175	0.000175	Up	Homo sapiens delta-notch-like EGF repeat-containing transmembrane (DNER), mRNA [NM_139072]
A_23_P23044	S100A9	1.922657	2.56E−05	0.000193	0.000193	Up	Homo sapiens S100 calcium binding protein A9 (calgranulin B) (S100A9), mRNA [NM_002965]
A_23_P127033	ECHDC3	1.578045	2.73E−05	0.000204	0.000204	Up	Homo sapiens enoyl Coenzyme A hydratase domain containing 3 (ECHDC3), mRNA [NM_024693]
A_23_P82499	PEG10	2.028863	2.88E−05	0.000213	0.000213	Up	Homo sapiens MEF3L1 mRNA for MEF3 like 1, complete cds. [AB049150]
A_23_P62807	CGI-49	1.37877	3.14E−05	0.00023	0.00023	Up	Homo sapiens CGI-49 protein (CGI-49), mRNA [NM_016002]
A_23_P20392	PSD3	1.487471	3.24E−05	0.000236	0.000236	Up	Homo sapiens pleckstrin and Sec7 domain containing 3, mRNA (cDNA clone IMAGE:4153308), complete cds. [BC011238]
A_23_P119642	ATP4A	2.182096	4.71E−05	0.000324	0.000324	Up	Homo sapiens ATPase, H+/K+exchanging, alpha polypeptide (ATP4A), mRNA [NM_000704]
A_23_P41789	SLC27A6	1.623705	4.71E−05	0.000324	0.000324	Up	Homo sapiens solute carrier family 27 (fatty acid transporter), member 6 (SLC27A6), mRNA [NM_014031]
A_23_P104492	PAPSS2	1.584993	5.07E−05	0.000345	0.000345	Up	Homo sapiens 3′-phosphoadenosine 5′-phosphosulfate synthase 2 (PAPSS2), mRNA [NM_004670]
A_23_P147404	#N/A	1.495452	5.14E−05	0.000349	0.000349	Up	Unknown
A_23_P430728	ATP4A	2.124477	5.44E−05	0.000367	0.000367	Up	Homo sapiens ATPase, H+/K+exchanging, alpha polypeptide (ATP4A), mRNA [NM_000704]
A_23_P92983	BHMT2	1.352067	5.46E−05	0.000368	0.000368	Up	Homo sapiens betaine-homocysteinemethyltransferase 2 (BHMT2), mRNA [NM_017614]
A_23_P300600	NEFH	1.514433	5.66E−05	0.000379	0.000379	Up	Homo sapiens neurofilament, heavy polypeptide 200 kDa (NEFH), mRNA [NM_021076]
A_23_P214080	EGR1	1.501231	7.23E−05	0.000464	0.000464	Up	Homo sapiens early growth response 1 (EGR1), mRNA [NM_001964]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P16523	GDF15	2.338168	9.47E−05	0.000586	0.000586	Up	Homo sapiens growth differentiation factor 15 (GDF15), mRNA [NM_004864]
A_23_P22526	HEPH	1.344565	0.000121	0.000721	0.000721	Up	Homo sapiens hephaestin (HEPH), transcript variant 2, mRNA [NM_014799]
A_23_P643	THC2160735	1.487481	0.000123	0.00073	0.00073	Up	Q8BIY2 (Q8BIY2) Musmusculus 10 days lactation, adult female mammary gland cDNA, RIKEN full-length enriched library, clone:D730020K15 product:HRIHFB2003 PROTEIN homolog, partial (31%) [THC2160735]
A_23_P121533	SPON2	1.743232	0.000126	0.000748	0.000748	Up	Homo sapiens spondin 2, extracellular matrix protein (SPON2), mRNA [NM_012445]
A_23_P383819	TBX3	1.365874	0.00013	0.000768	0.000768	Up	Homo sapiens T-box 3 (ulnar mammary syndrome) (TBX3), transcript variant 2, mRNA [NM_016569]
A_23_P408249	PCK1	1.934773	0.000145	0.000844	0.000844	Up	Homo sapiens phosphoenolpyruvatecarboxykinase 1 (soluble) (PCK1), mRNA [NM_002591]
A_23_P134237	RARRES2	1.894554	0.00015	0.000869	0.000869	Up	Homo sapiens retinoic acid receptor responder (tazarotene induced) 2 (RARRES2), mRNA [NM_002889]
A_23_P42975	PRKAR2B	1.373355	0.000151	0.000872	0.000872	Up	Homo sapiens protein kinase, cAMP-dependent, regulatory, type II, beta (PRKAR2B), mRNA [NM_002736]
A_23_P501007	EFEMP1	1.598832	0.000183	0.001027	0.001027	Up	Homo sapiens EGF-containing fibulin-like extracellular matrix protein 1 (EFEMP1), transcript variant 1, mRNA [NM_004105]
A_23_P119943	IGFBP2	1.373226	0.000203	0.001124	0.001124	Up	Homo sapiens insulin-like growth factor binding protein 2, 36 kDa (IGFBP2), mRNA [NM_000597]
A_23_P345733	MT1K	1.685593	0.000246	0.001333	0.001333	Up	Homo sapiens metallothionein 1 K (MT1 K), mRNA [NM_176870]
A_23_P206760	HP	2.100676	0.000276	0.001467	0.001467	Up	Homo sapiens haptoglobin (HP), mRNA [NM_005143]
A_23_P164057	MFAP4	1.473101	0.000629	0.002957	0.002957	Up	Homo sapiens microfibrillar-associated protein 4 (MFAP4), mRNA [NM_002404]
A_23_P99063	LUM	1.964127	0.000768	0.003494	0.003494	Up	Homo sapiens lumican (LUM), mRNA [NM_002345]
A_23_P315364	CXCL2	1.628551	0.000889	0.003946	0.003946	Up	Homo sapiens chemokine (C-X-C motif) ligand 2 (CXCL2), mRNA [NM_002089]
A_23_P2492	C1S	1.450737	0.00143	0.005882	0.005882	Up	Homo sapiens complement component 1, s subcomponent (C1S), transcript variant 1, mRNA [NM_001734]
A_23_P345128	SAA1	1.741685	0.002757	0.009989	0.009989	Up	Homo sapiens serum amyloid A1 (SAA1), transcript variant 1, mRNA [NM_000331]
A_23_P124905	NPTX1	1.461304	0.018037	0.045168	0.045168	Up	Homo sapiens neuronal pentraxin I (NPTX1), mRNA [NM_002522]
A_23_P120502	C20orf46	−2.44724	2E−17	5.51E−15	5.51E−15	Down	Homo sapiens chromosome 20 open reading frame 46 (C20orf46), mRNA [NM_018354]
A_23_P14062	NUP107	−1.48545	3.46E−16	7.05E−14	7.05E−14	Down	Homo sapiens nucleoporin 107 kDa (NUP107), mRNA [NM_020401]
A_23_P92765	CCDC112	−1.31485	1.14E−15	1.98E−13	1.98E−13	Down	Coiled-coil domain containing 112
A_23_P43675	ZNF618	−1.60896	2.28E−15	3.46E−13	3.46E−13	Down	Homo sapiens mRNA for KIAA1952 protein. [AB075832]
A_23_P148519	TMEM29	−1.55989	2.38E−14	2.8E−12	2.8E−12	Down	Homo sapiens transmembrane protein 29 (TMEM29), mRNA [NM_014138]
A_23_P50108	KNTC2	−2.89465	6.5E−14	6.63E−12	6.63E−12	Down	Homo sapiens kinetochore associated 2 (KNTC2), mRNA [NM_006101]
A_23_P39116	LIG1	−2.00847	1.49E−13	1.32E−11	1.32E−11	Down	Homo sapiens ligase I, DNA, ATP-dependent (LIG1), mRNA [NM_000234]
A_23_P76718	NEK3	−1.11789	1.76E−13	1.55E−11	1.55E−11	Down	Homo sapiens NIMA (never in mitosis gene a)-related kinase 3 (NEK3), transcript variant 1, mRNA [NM_002498]
A_23_P122007	C5ORF30	−1.55585	1.95E−13	1.69E−11	1.69E−11	Down	Chromosome 5 open reading frame 30
A_23_P90088	ZNF443	−1.04241	3.87E−13	3.1E−11	3.1E−11	Down	Homo sapiens zinc finger protein 443 (ZNF443), mRNA [NM_005815]
A_23_P102571	SLC2A4RG	−2.24304	4.87E−13	3.79E−11	3.79E−11	Down	Homo sapiens SLC2A4 regulator (SLC2A4RG), mRNA [NM_020062]
A_23_P54617	KIF22	−1.28421	7.09E−13	5.34E−11	5.34E−11	Down	Homo sapiens kinesin family member 22 (KIF22), mRNA [NM_007317]
A_23_P155815	HCAP-G	−2.73764	9.68E−13	7.05E−11	7.05E−11	Down	Homo sapiens chromosome condensation protein G (HCAP-G), mRNA [NM_022346]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P71644	FANCG	−1.05785	1.39E−12	9.7E−11	9.7E−11	Down	Homo sapiens Fanconianemia, complementation group G (FANCG), mRNA [NM_004629]
A_23_P354297	CHTF18	−1.64953	1.78E−12	1.19E−10	1.19E−10	Down	Homo sapiens CTF18, chromosome transmission fidelity factor 18 homolog (S. cerevisiae) (CHTF18), mRNA [NM_022092]
A_23_P155765	HMGB2	−1.3912	2.01E−12	1.33E−10	1.33E−10	Down	Homo sapiens high-mobility group box 2 (HMGB2), mRNA [NM_002129]
A_23_P259641	EZH2	−1.7615	3.1E−12	1.94E−10	1.94E−10	Down	Homo sapiens enhancer of zeste homolog 2 (Drosophila) (EZH2), transcript variant 1, mRNA [NM_004456]
A_23_P53276	TIMELESS	−1.60347	3.32E−12	2.07E−10	2.07E−10	Down	Homo sapiens timeless homolog (Drosophila) (TIMELESS), mRNA [NM_003920]
A_23_P203891	NCOR2	−1.13067	4.17E−12	2.52E−10	2.52E−10	Down	Homo sapiens nuclear receptor co-repressor 2 (NCOR2), mRNA [NM_006312]
A_23_P28953	DNMT3B	−1.15812	4.48E−12	2.71E−10	2.71E−10	Down	Homo sapiens DNA (cytosine-5-)-methyltransferase 3 beta (DNMT3B), transcript variant 6, mRNA [NM_175850]
A_23_P397334	PAQR4	−1.50144	5.16E−12	3.07E−10	3.07E−10	Down	Homo sapiens progestin and adipoQ receptor family member IV (PAQR4), mRNA [NM_152341]
A_23_P153687	XRCC1	−1.22159	6.35E−12	3.68E−10	3.68E−10	Down	Homo sapiens X-ray repair complementing defective repair in Chinese hamster cells 1 (XRCC1), mRNA [NM_006297]
A_23_P55107	ULK2	−0.90307	9.25E−12	5.12E−10	5.12E−10	Down	Homo sapiens unc-51-like kinase 2 (C. elegans) (ULK2), mRNA [NM_014683]
A_23_P133123	GAJ	−2.23062	1.22E−11	6.53E−10	6.53E−10	Down	Homo sapiens GAJ protein (GAJ), mRNA [NM_032117]
A_23_P30243	LRAP	−2.02657	1.27E−11	6.72E−10	6.72E−10	Down	Homo sapiens leukocyte-derived arginine aminopeptidase (LRAP), mRNA [NM_022350]
A_23_P305121	ANKRD23	−0.90049	1.31E−11	6.88E−10	6.88E−10	Down	Homo sapiens ankyrin repeat domain 23 (ANKRD23), mRNA [NM_144994]
A_23_P385861	CDCA2	−1.9254	2.4E−11	1.19E−09	1.19E−09	Down	Homo sapiens cell division cycle associated 2 (CDCA2), mRNA [NM_152562]
A_23_P103159	C22orf18	−1.57232	2.58E−11	1.27E−09	1.27E−09	Down	Homo sapiens chromosome 22 open reading frame 18 (C22orf18), transcript variant 1, mRNA [NM_024053]
A_23_P7636	PTTG1	−1.6619	3.27E−11	1.54E−09	1.54E−09	Down	Homo sapiens pituitary tumor-transforming 1 (PTTG1), mRNA [NM_004219]
A_23_P208896	CHAF1A	−1.30501	3.48E−11	1.63E−09	1.63E−09	Down	Homo sapiens chromatin assembly factor 1, subunit A (p150) (CHAF1A), mRNA [NM_005483]
A_23_P200829	SRGAP2	−1.42956	3.56E−11	1.66E−09	1.66E−09	Down	Homo sapiens mRNA for KIAA0456 protein, partial cds. [AB007925]
A_23_P4922ZSWIM9	ZSWIM9	−0.98242	4.31E−11	1.97E−09	1.97E−09	Down	Zinc finger SWIM-type containing 9
A_23_P250801	MCM2	−1.18518	4.49E−11	2.05E−09	2.05E−09	Down	Homo sapiens MCM2 minichromosome maintenance deficient 2, mitotin (S. cerevisiae) (MCM2), mRNA [NM_004526]
A_23_P170491	TRIP	−1.32102	4.85E−11	2.2E−09	2.2E−09	Down	Homo sapiens TRAF interacting protein (TRIP), mRNA [NM_005879]
A_23_P95302	RFC5	−1.27194	5.32E−11	2.38E−09	2.38E−09	Down	Homo sapiens replication factor C (activator 1) 5, 36.5 kDa (RFC5), transcript variant 2, mRNA [NM_181578]
A_23_P122197	CCNB1	−1.84758	5.34E−11	2.39E−09	2.39E−09	Down	Homo sapiens cyclin B1 (CCNB1), mRNA [NM_031966]
A_23_P118246	Pfs2	−1.39576	5.56E−11	2.48E−09	2.48E−09	Down	Homo sapiens DNA replication complex GINS protein PSF2 (Pfs2), mRNA [NM_016095]
A_23_P107764	ZNF266	−0.94393	5.61E−11	2.49E−09	2.49E−09	Down	Homo sapiens zinc finger protein 266 (ZNF266), mRNA [NM_006631]
A_23_P401	CENPF	−2.11932	5.85E−11	2.59E−09	2.59E−09	Down	Homo sapiens centromere protein F, 350/400 ka (mitosin) (CENPF), mRNA [NM_016343]
A_23_P90612	MCM6	−1.36868	6.96E−11	2.99E−09	2.99E−09	Down	Homo sapiens MCM6 minichromosome maintenance deficient 6 (MIS5 homolog, S. pombe) (S. cerevisiae) (MCM6), mRNA [NM_005915]
A_23_P145984	TM4SF12	−3.76051	7.04E−11	3.01E−09	3.01E−09	Down	Homo sapiens transmembrane 4 superfamily member 12 (TM4SF12), mRNA [NM_012338]
A_23_P157099	ANLN	−2.27002	7.33E−11	3.11E−09	3.11E−09	Down	Homo sapiens anillin, actin binding protein (scraps homolog, Drosophila) (ANLN), mRNA [NM_018685]
A_23_P159986	MIR503HG	−2.50886	8.32E−11	3.45E−09	3.45E−09	Down	MIR503 host gene
A_23_P254733	MLF1IP	−2.00923	8.56E−11	3.52E−09	3.52E−09	Down	Homo sapiens MLF1 interacting protein (MLF1IP), mRNA [NM_024629]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P87810	MAPKAPK5	− 1.19572	9.33E−11	3.81E−09	3.81E−09	Down	Mitogen-activated protein kinase-activated protein kinase 5
A_23_P67771	BARD1	− 1.11797	1.09E−10	4.39E−09	4.39E−09	Down	Homo sapiens BRCA1 associated RING domain 1 (BARD1), mRNA [NM_000465]
A_23_P136817	KNTC1	− 1.24621	1.43E−10	5.56E−09	5.56E−09	Down	Homo sapiens kinetochore associated 1 (KNTC1), mRNA [NM_014708]
A_23_P118815	BIRC5	− 2.45776	1.51E−10	5.85E−09	5.85E−09	Down	Homo sapiens baculoviral IAP repeat-containing 5 (survivin) (BIRC5), mRNA [NM_001168]
A_23_P48029	CLECSF6	− 1.29785	1.51E−10	5.86E−09	5.86E−09	Down	Homo sapiens C-type (calcium-dependent, carbohydrate-recognition domain) lectin, superfamily member 6 (CLECSF6), transcript variant 1, mRNA [NM_016184]
A_23_P253012	GRAMD1C	− 2.28854	1.55E−10	5.96E−09	5.96E−09	Down	GRAM domain containing 1C
A_23_P429461	FUK	− 1.07732	2.1E−10	7.9E−09	7.9E−09	Down	Homo sapiens fucokinase (FUK), mRNA [NM_145059]
A_23_P39574	CCDC150	− 0.94155	2.37E−10	8.77E−09	8.77E−09	Down	Coiled-coil domain containing 150
A_23_P80902	KNSL7	− 0.9483	2.65E−10	9.69E−09	9.69E−09	Down	Homo sapiens kinesin-like 7 (KNSL7), mRNA [NM_020242]
A_23_P61886	TM4SF9	− 1.47399	2.86E−10	1.04E−08	1.04E−08	Down	Homo sapiens cDNA FLJ31097 fis, clone IMR321000210. [AK055659]
A_23_P154730	ZNF133	− 1.11442	2.96E−10	1.08E−08	1.08E−08	Down	Homo sapiens zinc finger protein 133 (clone pHZ-13) (ZNF133), mRNA [NM_003434]
A_23_P122052	GPX8	− 1.96225	3.03E−10	1.09E−08	1.09E−08	Down	Glutathione peroxidase 8 (putative)
A_23_P50096	TYMS	− 2.8882	3.04E−10	1.09E−08	1.09E−08	Down	Homo sapiens thymidylatesynthetase (TYMS), mRNA [NM_001071]
A_23_P431378	C14orf80	− 0.91453	3.15E−10	1.13E−08	1.13E−08	Down	Homo sapiens chromosome 14 open reading frame 80 (C14orf80), mRNA [NM_173608]
A_23_P419213	KIAA1407	− 0.90946	3.61E−10	1.27E−08	1.27E−08	Down	Homo sapiens KIAA1407 (KIAA1407), mRNA [NM_020817]
A_23_P204048	DYRK2	− 1.00476	3.94E−10	1.38E−08	1.38E−08	Down	Homo sapiens dual specificity tyrosine-(Y)-phosphorylation regulated kinase 2 (DYRK2), transcript variant 2, mRNA [NM_006482]
A_23_P14184	THSD1	− 1.28532	4.1E−10	1.43E−08	1.43E−08	Down	Homo sapiens thrombospondin, type I, domain containing 1 (THSD1), transcript variant 1, mRNA [NM_018676]
A_23_P500390	DONSON	− 1.40903	4.41E−10	1.52E−08	1.52E−08	Down	Homo sapiens downstream neighbor of SON (DONSON), transcript variant 1, mRNA [NM_017613]
A_23_P379645	BMF	− 1.18785	4.69E−10	1.61E−08	1.61E−08	Down	Homo sapiens Bcl2 modifying factor (BMF), transcript variant 2, mRNA [NM_033503]
A_23_P356684	ANLN	− 1.98076	4.76E−10	1.64E−08	1.64E−08	Down	Homo sapiens anillin, actin binding protein (scraps homolog, Drosophila) (ANLN), mRNA [NM_018685]
A_23_P27638	ZNF700	− 0.89949	5.69E−10	1.92E−08	1.92E−08	Down	Zinc finger protein 700
A_23_P329271	MC1R	− 1.41083	5.74E−10	1.93E−08	1.93E−08	Down	Homo sapiens melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor) (MC1R), mRNA [NM_002386]
A_23_P74115	RAD54L	− 1.39824	6.12E−10	2.04E−08	2.04E−08	Down	Homo sapiens RAD54-like (S. cerevisiae) (RAD54L), mRNA [NM_003579]
A_23_P110742	THOC3	− 1.52507	6.74E−10	2.22E−08	2.22E−08	Down	Homo sapiens THO complex 3 (THOC3), mRNA [NM_032361]
A_23_P213592	RNF44	− 1.20365	7.67E−10	2.48E−08	2.48E−08	Down	Homo sapiens ring finger protein 44 (RNF44), mRNA [NM_014901]
A_23_P134295	NUDT1	− 1.1575	9.63E−10	2.98E−08	2.98E−08	Down	Homo sapiens nudix (nucleoside diphosphate linked moiety X)-type motif 1 (NUDT1), transcript variant 1, mRNA [NM_002452]
A_23_P386241	C20orf55	− 0.89957	9.66E−10	2.98E−08	2.98E−08	Down	Homo sapiens chromosome 20 open reading frame 55 (C20orf55), transcript variant 1, mRNA [NM_031424]
A_23_P301981	FLJ25402	− 0.93731	1.05E−09	3.19E−08	3.19E−08	Down	Homo sapiens hypothetical protein FLJ25402 (FLJ25402), mRNA [NM_001007090]
A_23_P65110	RACGAP1	− 1.88221	1.19E−09	3.54E−08	3.54E−08	Down	Homo sapiens RacGTPase activating protein 1 (RACGAP1), mRNA [NM_013277]
A_23_P74349	CDCA1	− 2.09628	1.19E−09	3.54E−08	3.54E−08	Down	Homo sapiens cell division cycle associated 1 (CDCA1), transcript variant 1, mRNA [NM_145697]
A_23_P8663	DMTF1	− 0.89863	1.36E−09	3.98E−08	3.98E−08	Down	Homo sapiens cyclin D binding myb-like transcription factor 1 (DMTF1), mRNA [NM_021145]
A_23_P154962	KIAA1666	− 1.14506	1.48E−09	4.27E−08	4.27E−08	Down	Homo sapiens mRNA; cDNA DKFZp434H0735 (from clone DKFZp434H0735). [AL117509]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P353717	MGC24665	− 1.42945	1.62E−09	4.63E−08	4.63E−08	Down	Homo sapiens hypothetical protein MGC24665 (MGC24665), mRNA [NM_152308]
A_23_P143147	TCFL5	− 1.23055	1.66E−09	4.71E−08	4.71E−08	Down	Homo sapiens transcription factor-like 5 (basic helix-loop-helix) (TCFL5), mRNA [NM_006602]
A_23_P93032	ZBED3	− 0.90063	1.66E−09	4.72E−08	4.72E−08	Down	Homo sapiens zinc finger, BED domain containing 3 (ZBED3), mRNA [NM_032367]
A_23_P99204	MAPKAPK5-AS1	− 1.0082	1.81E−09	5.1E−08	5.1E−08	Down	MAPKAPK5 antisense RNA 1
A_23_P206059	PRC1	− 1.23885	1.94E−09	5.42E−08	5.42E−08	Down	Homo sapiens protein regulator of cytokinesis 1 (PRC1), transcript variant 1, mRNA [NM_003981]
A_23_P89709	Cep192	− 1.23497	1.99E−09	5.56E−08	5.56E−08	Down	Homo sapiens centrosomal protein 192 kDa (Cep192), transcript variant 2, mRNA [NM_018069]
A_23_P104651	CDCA5	− 1.80764	2.1E−09	5.83E−08	5.83E−08	Down	Homo sapiens cell division cycle associated 5 (CDCA5), mRNA [NM_080668]
A_23_P52017	ASPM	− 1.94756	2.3E−09	6.3E−08	6.3E−08	Down	Homo sapiens asp (abnormal spindle)-like, microcephaly associated (Drosophila) (ASPM), mRNA [NM_018136]
A_23_P259135	NCOA6	− 1.08557	2.34E−09	6.39E−08	6.39E−08	Down	Homo sapiens nuclear receptor coactivator 6 (NCOA6), mRNA [NM_014071]
A_23_P257242	KIAA0922	− 1.32224	2.51E−09	6.77E−08	6.77E−08	Down	Homo sapiens KIAA0922 protein (KIAA0922), mRNA [NM_015196]
A_23_P60024	PTTG1	− 1.38718	2.65E−09	7.08E−08	7.08E−08	Down	Homo sapiens pituitary tumor-transforming 1 (PTTG1), mRNA [NM_004219]
A_23_P6582	BX537558	− 1.01523	3.03E−09	7.97E−08	7.97E−08	Down	Homo sapiens mRNA; cDNA DKFZp686J1569 (from clone DKFZp686J1569). [BX537558]
A_23_P136222	RRM2	− 1.43172	3.06E−09	8.03E−08	8.03E−08	Down	Homo sapiens ribonucleotidereductase M2 polypeptide (RRM2), mRNA [NM_001034]
A_23_P63789	ZWINT	− 1.61815	3.22E−09	8.39E−08	8.39E−08	Down	Homo sapiens ZW10 interactor (ZWINT), transcript variant 2, mRNA [NM_032997]
A_23_P204689	OCIL	− 0.93413	3.58E−09	9.25E−08	9.25E−08	Down	Homo sapiens lectin-like NK cell receptor (OCIL), transcript variant 1, mRNA [NM_013269]
A_23_P253281	TBC1D8	− 1.54819	3.92E−09	1E−07	1E−07	Down	Homo sapiens TBC1 domain family, member 8 (with GRAM domain) (TBC1D8), mRNA [NM_007063]
A_23_P18196	RFC4	− 1.39651	4.03E−09	1.03E−07	1.03E−07	Down	Homo sapiens replication factor C (activator 1) 4, 37 kDa (RFC4), transcript variant 1, mRNA [NM_002916]
A_23_P254441	LOC155060	− 1.16606	4.16E−09	1.06E−07	1.06E−07	Down	Homo sapiens hypothetical protein LOC155060 (LOC155060), mRNA [NM_001004302]
A_23_P45365	COL4A5	− 1.77724	4.43E−09	1.12E−07	1.12E−07	Down	Homo sapiens collagen, type IV, alpha 5 (Alport syndrome) (COL4A5), transcript variant 2, mRNA [NM_033380]
A_23_P124417	BUB1	− 1.4823	4.76E−09	1.19E−07	1.19E−07	Down	Homo sapiens BUB1 budding uninhibited by benzimidazoles 1 homolog (yeast) (BUB1), mRNA [NM_004336]
A_23_P372984	MGC24975	− 1.21031	5.97E−09	1.45E−07	1.45E−07	Down	Homo sapiens hypothetical protein MGC24975 (MGC24975), mRNA [NM_153359]
A_23_P163546	TAF1C	− 0.99394	5.98E−09	1.45E−07	1.45E−07	Down	Homo sapiens TATA box binding protein (TBP)-associated factor, RNA polymerase I, C, 110 kDa (TAF1C), transcript variant 1, mRNA [NM_005679]
A_23_P19102	GALNT10	− 0.9915	6.18E−09	1.49E−07	1.49E−07	Down	Homo sapiens cDNA FLJ11715 fis, clone HEMBA1005223. [AK021777]
A_23_P155989	FKSG14	− 1.38224	6.21E−09	1.5E−07	1.5E−07	Down	Homo sapiens leucine zipper protein FKSG14 (FKSG14), mRNA [NM_022145]
A_23_P253752	FAM54A	− 1.33666	6.97E−09	1.65E−07	1.65E−07	Down	Homo sapiens family with sequence similarity 54, member A (FAM54A), mRNA [NM_138419]
A_23_P210482	ADA	− 0.99832	8.29E−09	1.92E−07	1.92E−07	Down	Homo sapiens adenosine deaminase (ADA), mRNA [NM_000022]
A_23_P304420	TIGD2	− 0.92411	8.59E−09	1.98E−07	1.98E−07	Down	Homo sapiens tigger transposable element derived 2 (TIGD2), mRNA [NM_145715]
A_23_P102471	MSH2	− 1.01241	8.78E−09	2.01E−07	2.01E−07	Down	Homo sapiens mutS homolog 2, colon cancer, nonpolyposis type 1 (E. coli) (MSH2), mRNA [NM_000251]
A_23_P415443	BRRN1	− 1.07647	9.48E−09	2.13E−07	2.13E−07	Down	Homo sapiens barren homolog (Drosophila) (BRRN1), mRNA [NM_015341]
A_23_P117852	KIAA0101	− 2.04411	9.48E−09	2.13E−07	2.13E−07	Down	Homo sapiens KIAA0101 (KIAA0101), mRNA [NM_014736]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P118582	TBPIP	−1.17055	9.83E−09	2.2E−07	2.2E−07	Down	Homo sapiens TBP-1 interacting protein (TBPIP), mRNA [NM_013290]
A_23_P49878	PIMREG	−1.42283	1.06E−08	2.33E−07	2.33E−07	Down	PICALM interacting mitotic regulator
A_23_P49546	GRIN2C	−2.64708	1.15E−08	2.52E−07	2.52E−07	Down	Homo sapiens glutamate receptor, ionotropic, *N*-methyl D-aspartate 2C (GRIN2C), mRNA [NM_000835]
A_23_P169518	RABEP2	−1.31326	1.25E−08	2.71E−07	2.71E−07	Down	Homo sapiens rabaptin, RAB GTPase binding effector protein 2 (RABEP2), mRNA [NM_024816]
A_23_P166336	TMEM191A	−1.58475	1.25E−08	2.71E−07	2.71E−07	Down	transmembrane protein 191A (pseudogene)
A_23_P107421	TK1	−1.87477	1.27E−08	2.75E−07	2.75E−07	Down	Homo sapiens thymidine kinase 1, soluble (TK1), mRNA [NM_003258]
A_23_P209032	ZNF302	−0.99579	1.39E−08	2.98E−07	2.98E−07	Down	Homo sapiens zinc finger protein 302 (ZNF302), mRNA [NM_018675]
A_23_P129577	TIGD7	−1.03443	1.4E−08	2.98E−07	2.98E−07	Down	Homo sapiens tigger transposable element derived 7 (TIGD7), mRNA [NM_033208]
A_23_P384056	CCDC14	−0.96808	1.44E−08	3.06E−07	3.06E−07	Down	Homo sapiens hypothetical protein FLJ12892 (FLJ12892), mRNA [NM_022757]
A_23_P129014	C14orf143	−1.04737	1.57E−08	3.3E−07	3.3E−07	Down	Homo sapiens chromosome 14 open reading frame 143 (C14orf143), mRNA [NM_145231]
A_23_P145016	BRD8	−1.13016	1.61E−08	3.37E−07	3.37E−07	Down	Homo sapiens bromodomain containing 8 (BRD8), transcript variant 1, mRNA [NM_006696]
A_23_P15582	XYLT2	−1.0013	1.67E−08	3.48E−07	3.48E−07	Down	Homo sapiens xylosyltransferase II (XYLT2), mRNA [NM_022167]
A_23_P259586	TTK	−1.45244	1.71E−08	3.57E−07	3.57E−07	Down	Homo sapiens TTK protein kinase (TTK), mRNA [NM_003318]
A_23_P57306	CHAF1B	−1.29456	1.98E−08	4.06E−07	4.06E−07	Down	Homo sapiens chromatin assembly factor 1, subunit B (p60) (CHAF1B), mRNA [NM_005441]
A_23_P37776	FHOD1	−0.8996	2.06E−08	4.2E−07	4.2E−07	Down	Homo sapiens formin homology 2 domain containing 1 (FHOD1), mRNA [NM_013241]
A_23_P134650	PTCD1	−0.90704	2.07E−08	4.21E−07	4.21E−07	Down	Homo sapiens pentatricopeptide repeat domain 1 (PTCD1), mRNA [NM_015545]
A_23_P88731	RAD51	−1.18403	2.11E−08	4.29E−07	4.29E−07	Down	Homo sapiens RAD51 homolog (RecA homolog, E. coli) (S. cerevisiae) (RAD51), transcript variant 1, mRNA [NM_002875]
A_23_P168882	TP53INP1	−0.96853	2.12E−08	4.3E−07	4.3E−07	Down	Homo sapiens tumor protein p53 inducible nuclear protein 1 (TP53INP1), mRNA [NM_033285]
A_23_P10385	RAMP	−1.00077	2.26E−08	4.52E−07	4.52E−07	Down	Homo sapiens RA-regulated nuclear matrix-associated protein (RAMP), mRNA [NM_016448]
A_23_P52589	C11orf13	−1.2586	2.34E−08	4.65E−07	4.65E−07	Down	Homo sapiens chromosome 11 open reading frame 13 (C11orf13), mRNA [NM_003475]
A_23_P87769	FLJ20641	−1.14319	2.44E−08	4.83E−07	4.83E−07	Down	Homo sapiens hypothetical protein FLJ20641 (FLJ20641), mRNA [NM_017915]
A_23_P4626	ZNF606	−0.92907	2.61E−08	5.12E−07	5.12E−07	Down	Homo sapiens zinc finger protein 606 (ZNF606), mRNA [NM_025027]
A_23_P215525	OSBPL3	−1.27972	2.83E−08	5.51E−07	5.51E−07	Down	Homo sapiens oxysterol binding protein-like 3 (OSBPL3), transcript variant 5, mRNA [NM_145323]
A_23_P146456	CTSL2	−1.86176	3E−08	5.79E−07	5.79E−07	Down	Homo sapiens cathepsin L2 (CTSL2), mRNA [NM_001333]
A_23_P82699	PBK	−1.82906	3.3E−08	6.3E−07	6.3E−07	Down	Homo sapiens PDZ binding kinase (PBK), mRNA [NM_018492]
A_23_P408108	MTERF	−0.9142	3.82E−08	7.15E−07	7.15E−07	Down	Homo sapiens transcription termination factor, mitochondrial (MTERF), nuclear gene encoding mitochondrial protein, mRNA [NM_006980]
A_23_P214059	NR3C1	−1.02608	4.27E−08	7.89E−07	7.89E−07	Down	Homo sapiens nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor) (NR3C1), mRNA [NM_000176]
A_23_P303876	APOBEC3A	−1.07229	5.18E−08	9.38E−07	9.38E−07	Down	Homo sapiens apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3A (APOBEC3A), mRNA [NM_145699]
A_23_P138507	CDC2	−1.75136	5.21E−08	9.41E−07	9.41E−07	Down	Homo sapiens cell division cycle 2, G1 to S and G2 to M (CDC2), transcript variant 1, mRNA [NM_001786]
A_23_P168771	KIAA1505	−1.02657	5.28E−08	9.52E−07	9.52E−07	Down	Homo sapiens KIAA1505 protein (KIAA1505), mRNA [NM_020879]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P43595	KIF24	− 1.04984	5.65E−08	1.01E−06	1.01E−06	Down	Homo sapiens cDNA FLJ10933 fis, clone OVARC1000605. [AK001795]
A_23_P151405	CKAP2	− 1.41557	5.78E−08	1.03E−06	1.03E−06	Down	Homo sapiens cytoskeleton associated protein 2 (CKAP2), mRNA [NM_018204]
A_23_P88331	DLG7	− 1.58279	5.8E−08	1.04E−06	1.04E−06	Down	Homo sapiens discs, large homolog 7 (Drosophila) (DLG7), mRNA [NM_014750]
A_23_P323930	TM4SF9	− 1.10212	6.09E−08	1.08E−06	1.08E−06	Down	Homo sapiens transmembrane 4 superfamily member 9 (TM4SF9), mRNA [NM_005723]
A_23_P160427	FLJ14146	− 1.47335	7.1E−08	1.23E−06	1.23E−06	Down	Homo sapiens hypothetical protein FLJ14146 (FLJ14146), mRNA [NM_024709]
A_23_P382775	BBC3	− 1.80948	7.15E−08	1.24E−06	1.24E−06	Down	Homo sapiens BCL2 binding component 3 (BBC3), mRNA [NM_014417]
A_23_P103765	FCER1A	− 1.92634	7.33E−08	1.26E−06	1.26E−06	Down	Homo sapiens Fc fragment of IgE, high affinity I, receptor for; alpha polypeptide (FCER1A), mRNA [NM_002001]
A_23_P217755	APXL	− 0.89187	7.46E−08	1.28E−06	1.28E−06	Down	Homo sapiens apical protein-like (Xenopuslaevis) (APXL), mRNA [NM_001649]
A_23_P334192	FLJ90709	− 0.90236	7.58E−08	1.3E−06	1.3E−06	Down	Homo sapiens hypothetical protein FLJ90709 (FLJ90709), mRNA [NM_173514]
A_23_P145657	STAG3	− 1.57565	8.01E−08	1.36E−06	1.36E−06	Down	Homo sapiens stromal antigen 3 (STAG3), mRNA [NM_012447]
A_23_P92441	MAD2L1	− 1.83703	8.8E−08	1.48E−06	1.48E−06	Down	Homo sapiens MAD2 mitotic arrest deficient-like 1 (yeast) (MAD2L1), mRNA [NM_002358]
A_23_P335898	STK36	− 1.00524	9.22E−08	1.53E−06	1.53E−06	Down	Homo sapiens serine/threonine kinase 36 (fused homolog, Drosophila) (STK36), mRNA [NM_015690]
A_23_P134684	HMBOX1	− 1.67613	9.84E−08	1.62E−06	1.62E−06	Down	Homeobox containing 1
A_23_P419712	BTBD11	− 1.60242	1.08E−07	1.76E−06	1.76E−06	Down	Homo sapiens BTB (POZ) domain containing 11 (BTBD11), mRNA [NM_152322]
A_23_P57379	CDC45L	− 0.99332	1.1E−07	1.79E−06	1.79E−06	Down	Homo sapiens CDC45 cell division cycle 45-like (S. cerevisiae) (CDC45L), mRNA [NM_003504]
A_23_P7873	MCM3	− 1.06224	1.18E−07	1.91E−06	1.91E−06	Down	Homo sapiens MCM3 minichromosome maintenance deficient 3 (S. cerevisiae) (MCM3), mRNA [NM_002388]
A_23_P30805	HIST1H4J	− 1.09383	1.19E−07	1.93E−06	1.93E−06	Down	Homo sapiens histone 1, H4j (HIST1H4J), mRNA [NM_021968]
A_23_P118834	TOP2A	− 1.56004	1.19E−07	1.93E−06	1.93E−06	Down	Homo sapiens topoisomerase (DNA) II alpha 170 kDa (TOP2A), mRNA [NM_001067]
A_23_P76998	KIAA1036	− 0.90919	1.24E−07	2E−06	2E−06	Down	Homo sapiens KIAA1036 (KIAA1036), mRNA [NM_014909]
A_23_P210827	C20orf36	− 0.98887	1.26E−07	2.02E−06	2.02E−06	Down	Homo sapiens chromosome 20 open reading frame 36 (C20orf36), mRNA [NM_018257]
A_23_P65757	CCNB2	− 1.90059	1.28E−07	2.06E−06	2.06E−06	Down	Homo sapiens cyclin B2 (CCNB2), mRNA [NM_004701]
A_23_P92860	UNG2	− 1.25246	1.31E−07	2.1E−06	2.1E−06	Down	Homo sapiens uracil-DNA glycosylase 2 (UNG2), mRNA [NM_021147]
A_23_P72551	ULK1	− 1.11303	1.39E−07	2.22E−06	2.22E−06	Down	Homo sapiens unc-51-like kinase 1 (C. elegans) (ULK1), mRNA [NM_003565]
A_23_P149535	SLC27A3	− 0.94076	1.4E−07	2.23E−06	2.23E−06	Down	Homo sapiens solute carrier family 27 (fatty acid transporter), member 3 (SLC27A3), mRNA [NM_024330]
A_23_P215634	IGFBP3	− 1.71913	1.43E−07	2.26E−06	2.26E−06	Down	Homo sapiens insulin-like growth factor binding protein 3 (IGFBP3), mRNA [NM_000598]
A_23_P381979	OGT	− 1.40304	1.51E−07	2.37E−06	2.37E−06	Down	Homo sapiens O-linked *N*-acetylglucosamine (GlcNAc) transferase (UDP-*N*-acetylglucosamine:polypeptide-*N*-acetylglucosaminyltransferase) (OGT), transcript variant 3, mRNA [NM_003605]
A_23_P435636	DAND5	− 1.1108	1.51E−07	2.38E−06	2.38E−06	Down	Homo sapiens DAN domain family, member 5 (DAND5), mRNA [NM_152654]
A_23_P99292	RAD51AP1	− 1.07704	1.82E−07	2.78E−06	2.78E−06	Down	Homo sapiens RAD51 associated protein 1 (RAD51AP1), mRNA [NM_006479]
A_23_P98930	FLJ10652	− 0.9909	1.92E−07	2.9E−06	2.9E−06	Down	Homo sapiens hypothetical protein FLJ10652 (FLJ10652), mRNA [NM_018169]
A_23_P111112	VARS2L	− 0.94359	2.01E−07	3.01E−06	3.01E−06	Down	Homo sapiens valyl-tRNAsynthetase 2-like (VARS2L), mRNA [NM_020442]
A_23_P156417	CAP2	− 1.22678	2.19E−07	3.25E−06	3.25E−06	Down	Homo sapiens CAP, adenylatecyclase-associated protein, 2 (yeast) (CAP2), mRNA [NM_006366]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P94422	MELK	−1.48072	2.29E−07	3.39E−06	3.39E−06	Down	Homo sapiens maternal embryonic leucine zipper kinase (MELK), mRNA [NM_014791]
A_23_P54055	JUB	−1.33177	2.31E−07	3.41E−06	3.41E−06	Down	Homo sapiens jub, ajuba homolog (Xenopuslaevis) (JUB), transcript variant 1, mRNA [NM_032876]
A_23_P209200	CCNE1	−1.67389	2.32E−07	3.42E−06	3.42E−06	Down	Homo sapiens cyclin E1 (CCNE1), transcript variant 1, mRNA [NM_001238]
A_23_P89509	SPAG5	−1.34397	2.38E−07	3.5E−06	3.5E−06	Down	Homo sapiens sperm associated antigen 5 (SPAG5), mRNA [NM_006461]
A_23_P27023	RAB11FIP4	−1.94155	2.43E−07	3.56E−06	3.56E−06	Down	Homo sapiens RAB11 family interacting protein 4 (class II) (RAB11FIP4), mRNA [NM_032932]
A_23_P115482	HSPC150	−1.28962	2.49E−07	3.64E−06	3.64E−06	Down	Homo sapiens HSPC150 protein similar to ubiquitin-conjugating enzyme (HSPC150), mRNA [NM_014176]
A_23_P7596	MYO10	−1.59744	2.81E−07	4.05E−06	4.05E−06	Down	Homo sapiens myosin X (MYO10), mRNA [NM_012334]
A_23_P35219	NEK2	−1.07453	2.83E−07	4.07E−06	4.07E−06	Down	Homo sapiens NIMA (never in mitosis gene a)-related kinase 2 (NEK2), mRNA [NM_002497]
A_23_P68610	TPX2	−1.03148	2.98E−07	4.25E−06	4.25E−06	Down	Homo sapiens TPX2, microtubule-associated protein homolog (Xenopuslaevis) (TPX2), mRNA [NM_012112]
A_23_P64689	USP52	−0.92098	3E−07	4.27E−06	4.27E−06	Down	Homo sapiens ubiquitin specific protease 52 (USP52), mRNA [NM_014871]
A_23_P204158	RNFT2	−1.03854	3.19E−07	4.51E−06	4.51E−06	Down	Ring finger protein, transmembrane 2
A_23_P403334	SLAC2-B	−1.28188	3.32E−07	4.67E−06	4.67E−06	Down	Homo sapiens SLAC2-B (SLAC2-B), mRNA [NM_015065]
A_23_P85780	PHGDH	−0.94742	3.33E−07	4.67E−06	4.67E−06	Down	Homo sapiens phosphoglycerate dehydrogenase (PHGDH), mRNA [NM_006623]
A_23_P428840	TMEM44	−0.99297	3.37E−07	4.72E−06	4.72E−06	Down	Homo sapiens transmembrane protein 44 (TMEM44), transcript variant 1, mRNA [NM_138399]
A_23_P23611	AMY1A	−1.32504	3.58E−07	4.97E−06	4.97E−06	Down	Homo sapiens amylase, alpha 1A; salivary (AMY1A), transcript variant 1, mRNA [NM_004038]
A_23_P323751	C20orf129	−1.43523	3.59E−07	4.99E−06	4.99E−06	Down	Homo sapiens chromosome 20 open reading frame 129 (C20orf129), mRNA [NM_030919]
A_23_P110473	BIRC1	−1.07567	3.63E−07	5.04E−06	5.04E−06	Down	Homo sapiens baculoviral IAP repeat-containing 1 (BIRC1), mRNA [NM_004536]
A_23_P211926	WNT5A	−1.07553	3.96E−07	5.44E−06	5.44E−06	Down	Homo sapiens wingless-type MMTV integration site family, member 5A (WNT5A), mRNA [NM_003392]
A_23_P93311	DDR1	−0.90059	4E−07	5.48E−06	5.48E−06	Down	Homo sapiens discoidin domain receptor family, member 1 (DDR1), transcript variant 3, mRNA [NM_013994]
A_23_P253052	CD99L2	−0.93662	4.01E−07	5.49E−06	5.49E−06	Down	Homo sapiens CD99 antigen-like 2 (CD99L2), mRNA [NM_031462]
A_23_P60079	ANGPT2	−1.48846	4.04E−07	5.52E−06	5.52E−06	Down	Homo sapiens angiopoietin 2 (ANGPT2), mRNA [NM_001147]
A_23_P51085	Spc25	−1.22226	4.38E−07	5.91E−06	5.91E−06	Down	Homo sapiens kinetochore protein Spc25 (Spc25), mRNA [NM_020675]
A_23_P52278	KIF11	−0.92531	4.41E−07	5.93E−06	5.93E−06	Down	Homo sapiens kinesin family member 11 (KIF11), mRNA [NM_004523]
A_23_P50456	POLD1	−0.91621	4.41E−07	5.93E−06	5.93E−06	Down	Homo sapiens polymerase (DNA directed), delta 1, catalytic subunit 125 kDa (POLD1), mRNA [NM_002691]
A_23_P375	CDCA8	−0.909	4.51E−07	6.04E−06	6.04E−06	Down	Homo sapiens cell division cycle associated 8 (CDCA8), mRNA [NM_018101]
A_23_P161507	MTL5	−1.22381	4.86E−07	6.44E−06	6.44E−06	Down	Homo sapiens metallothionein-like 5, testis-specific (tesmin) (MTL5), mRNA [NM_004923]
A_23_P19712	GMNN	−1.17861	4.96E−07	6.56E−06	6.56E−06	Down	Homo sapiens geminin, DNA replication inhibitor (GMNN), mRNA [NM_015895]
A_23_P92794	C5orf13	−1.4605	5.51E−07	7.18E−06	7.18E−06	Down	Homo sapiens chromosome 5 open reading frame 13 (C5orf13), mRNA [NM_004772]
A_23_P111125	HCP5	−1.02701	5.54E−07	7.2E−06	7.2E−06	Down	Homo sapiens HLA complex P5 (HCP5), mRNA [NM_006674]
A_23_P501372	SMCR7	−0.9339	5.82E−07	7.51E−06	7.51E−06	Down	Homo sapiens Smith-Magenis syndrome chromosome region, candidate 7 (SMCR7), transcript variant 1, mRNA [NM_139162]
A_23_P86330	IER5	−0.931	6.3E−07	8.07E−06	8.07E−06	Down	Homo sapiens immediate early response 5 (IER5), mRNA [NM_016545]
A_23_P143184	MYBL2	−0.94048	6.36E−07	8.13E−06	8.13E−06	Down	Homo sapiens v-mybmyeloblastosis viral oncogene homolog (avian)-like 2 (MYBL2), mRNA [NM_002466]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P379614	OIP5	− 1.30725	6.49E−07	8.29E−06	8.29E−06	Down	Homo sapiens Opa interacting protein 5 (OIP5), mRNA [NM_007280]
A_23_P350689	ZDHHC23	− 0.92249	6.62E−07	8.43E−06	8.43E−06	Down	Homo sapiens zinc finger, DHHC domain containing 23 (ZDHHC23), mRNA [NM_173570]
A_23_P109539	APOBEC3B	− 1.94465	6.67E−07	8.47E−06	8.47E−06	Down	Homo sapiens apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3B (APOBEC3B), mRNA [NM_004900]
A_23_P89780	LAMA3	− 0.89893	6.86E−07	8.69E−06	8.69E−06	Down	Homo sapiens laminin, alpha 3 (LAMA3), transcript variant 2, mRNA [NM_000227]
A_23_P23303	EXO1	− 1.02968	7.3E−07	9.16E−06	9.16E−06	Down	Homo sapiens exonuclease 1 (EXO1), transcript variant 3, mRNA [NM_003686]
A_23_P27490	DNMT1	− 0.93477	7.49E−07	9.39E−06	9.39E−06	Down	Homo sapiens DNA (cytosine-5-)-methyltransferase 1 (DNMT1), mRNA [NM_001379]
A_23_P348298	SHD1	− 0.90022	7.57E−07	9.48E−06	9.48E−06	Down	Homo sapiens Sac3 homology domain 1 (S. cerevisiae) (SHD1), mRNA [NM_013299]
A_23_P115872	C10orf3	− 1.59407	8.01E−07	9.97E−06	9.97E−06	Down	Homo sapiens chromosome 10 open reading frame 3 (C10orf3), mRNA [NM_018131]
A_23_P33898	MAGED2	− 1.40465	8.82E−07	1.08E−05	1.08E−05	Down	Homo sapiens melanoma antigen family D, 2 (MAGED2), transcript variant 3, mRNA [NM_201222]
A_23_P94030	LAMB1	− 1.54566	9.28E−07	1.13E−05	1.13E−05	Down	Homo sapiens laminin, beta 1 (LAMB1), mRNA [NM_002291]
A_23_P323761	T3JAM	− 1.23091	1.01E−06	1.21E−05	1.21E−05	Down	Homo sapiens TRAF3-interacting Jun N-terminal kinase (JNK)-activating modulator (T3JAM), mRNA [NM_025228]
A_23_P70007	HMMR	− 1.08697	1.02E−06	1.23E−05	1.23E−05	Down	Homo sapiens hyaluronan-mediated motility receptor (RHAMM) (HMMR), transcript variant 1, mRNA [NM_012484]
A_23_P130376	FAM38B	− 1.46994	1.07E−06	1.28E−05	1.28E−05	Down	Homo sapiens family with sequence similarity 38, member B (FAM38B), mRNA [NM_022068]
A_23_P92719	RAI14	− 0.9475	1.08E−06	1.28E−05	1.28E−05	Down	Homo sapiens retinoic acid induced 14 (RAI14), mRNA [NM_015577]
A_23_P118203	ZG16B	− 1.98143	1.08E−06	1.28E−05	1.28E−05	Down	Zymogen granule protein 16B
A_23_P65918	ITPKA	− 1.22409	1.09E−06	1.29E−05	1.29E−05	Down	Homo sapiens inositol 1,4,5-trisphosphate 3-kinase A (ITPKA), mRNA [NM_002220]
A_23_P58819	RANBP17	− 1.01877	1.1E−06	1.31E−05	1.31E−05	Down	Homo sapiens RAN-binding protein 17 (RANBP17), mRNA [NM_022897]
A_23_P150667	KIF18A	− 1.06151	1.16E−06	1.37E−05	1.37E−05	Down	Homo sapiens kinesin family member 18A (KIF18A), mRNA [NM_031217]
A_23_P214281	C6orf33	− 1.00757	1.18E−06	1.39E−05	1.39E−05	Down	Homo sapiens chromosome 6 open reading frame 33 (C6orf33), mRNA [NM_133367]
A_23_P8013	HIST1H2BL	− 1.1994	1.26E−06	1.46E−05	1.46E−05	Down	Homo sapiens histone 1, H2bl (HIST1H2BL), mRNA [NM_003519]
A_23_P501435	CSRP2BP	− 0.92366	1.27E−06	1.47E−05	1.47E−05	Down	Homo sapiens CSRP2 binding protein (CSRP2BP), transcript variant 1, mRNA [NM_020536]
A_23_P88678	C15orf27	− 1.7115	1.28E−06	1.48E−05	1.48E−05	Down	Homo sapiens chromosome 15 open reading frame 27 (C15orf27), mRNA [NM_152335]
A_23_P402081	HIST1H2BN	− 0.98081	1.3E−06	1.49E−05	1.49E−05	Down	Homo sapiens histone 1, H2bn (HIST1H2BN), mRNA [NM_003520]
A_23_P167017	POPDC2	− 1.09466	1.37E−06	1.56E−05	1.56E−05	Down	Homo sapiens popeye domain containing 2 (POPDC2), mRNA [NM_022135]
A_23_P90333	ZNF404	− 2.16367	1.44E−06	1.63E−05	1.63E−05	Down	PREDICTED: Homo sapiens zinc finger protein 404 (ZNF404), mRNA [XM_292765]
A_23_P26883	MMP28	− 1.02264	1.44E−06	1.63E−05	1.63E−05	Down	Homo sapiens matrix metalloproteinase 28 (MMP28), transcript variant 2, mRNA [NM_032950]
A_23_P348257	ARK5	− 1.23185	1.45E−06	1.65E−05	1.65E−05	Down	Homo sapiens AMP-activated protein kinase family member 5 (ARK5), mRNA [NM_014840]
A_23_P3911	PLXDC1	− 1.24127	1.56E−06	1.76E−05	1.76E−05	Down	Homo sapiens plexin domain containing 1 (PLXDC1), mRNA [NM_020405]
A_23_P119095	PPP1R13L	− 0.91327	1.6E−06	1.79E−05	1.79E−05	Down	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 13 like (PPP1R13L), mRNA [NM_006663]
A_23_P47885	LRIG3	− 1.34385	1.63E−06	1.82E−05	1.82E−05	Down	Homo sapiens leucine-rich repeats and immunoglobulin-like domains 3 (LRIG3), mRNA [NM_153377]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P213424	ENC1	−1.43918	1.67E−06	1.85E−05	1.85E−05	Down	Homo sapiens ectodermal-neural cortex (with BTB-like domain) (ENC1), mRNA [NM_003633]
A_23_P217236	HMGB3	−1.20525	1.87E−06	2.04E−05	2.04E−05	Down	Homo sapiens high-mobility group box 3 (HMGB3), mRNA [NM_005342]
A_23_P140434	MYO5C	−1.06559	1.94E−06	2.11E−05	2.11E−05	Down	Homo sapiens myosin VC (MYO5C), mRNA [NM_018728]
A_23_P31677	MGC40214	−1.13403	1.95E−06	2.11E−05	2.11E−05	Down	Homo sapiens cDNA FLJ23887 fis, clone LNG14332. [AK074467]
A_23_P206441	FANCA	−0.96016	2.03E−06	2.18E−05	2.18E−05	Down	Homo sapiens Fanconianemia, complementation group A (FANCA), mRNA [NM_000135]
A_23_P253873	RAM2	−0.97246	2.06E−06	2.21E−05	2.21E−05	Down	Homo sapiens transcription factor RAM2 (RAM2), mRNA [NM_018719]
A_23_P68547	MCM8	−0.98892	2.13E−06	2.28E−05	2.28E−05	Down	Homo sapiens MCM8 minichromosome maintenance deficient 8 (S. cerevisiae) (MCM8), transcript variant 1, mRNA [NM_032485]
A_23_P24083	PNLIPRP2	−1.13262	2.14E−06	2.28E−05	2.28E−05	Down	Homo sapiens pancreatic lipase-related protein 2 (PNLIPRP2), mRNA [NM_005396]
A_23_P14986	HSD11B2	−0.98991	2.24E−06	2.38E−05	2.38E−05	Down	Homo sapiens hydroxysteroid (11-beta) dehydrogenase 2 (HSD11B2), mRNA [NM_000196]
A_23_P48669	CDKN3	−1.3619	2.34E−06	2.47E−05	2.47E−05	Down	Homo sapiens cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase) (CDKN3), mRNA [NM_005192]
A_23_P334608	GUSB	−0.89383	2.38E−06	2.5E−05	2.5E−05	Down	Homo sapiens glucuronidase, beta (GUSB), mRNA [NM_000181]
A_23_P79429	DKFZp762E1312	−1.08064	2.42E−06	2.54E−05	2.54E−05	Down	Homo sapiens hypothetical protein DKFZp762E1312 (DKFZp762E1312), mRNA [NM_018410]
A_23_P210191	U96396	−1.07648	2.42E−06	2.54E−05	2.54E−05	Down	Homo sapiens anti-streptococcal/anti-myosin immunoglobulin kappa light chain variable region mRNA, partial cds. [U96396]
A_23_P32661	#N/A	−0.90375	2.52E−06	2.64E−05	2.64E−05	Down	Unknown
A_23_P159011	#N/A	−1.47544	2.56E−06	2.67E−05	2.67E−05	Down	Unknown
A_23_P204630	NTN4	−1.2679	2.77E−06	2.88E−05	2.88E−05	Down	Homo sapiens netrin 4 (NTN4), mRNA [NM_021229]
A_23_P6741	IQSEC1	−1.06833	2.78E−06	2.89E−05	2.89E−05	Down	Homo sapiens IQ motif and Sec7 domain 1 (IQSEC1), mRNA [NM_014869]
A_23_P213050	HPGD	−1.26301	2.85E−06	2.94E−05	2.94E−05	Down	Homo sapiens hydroxyprostaglandin dehydrogenase 15-(NAD) (HPGD), mRNA [NM_000860]
A_23_P123276	FZD6	−0.89184	3E−06	3.07E−05	3.07E−05	Down	Homo sapiens frizzled homolog 6 (Drosophila) (FZD6), mRNA [NM_003506]
A_23_P251421	CDCA7	−1.2878	3.03E−06	3.09E−05	3.09E−05	Down	Homo sapiens cell division cycle associated 7 (CDCA7), transcript variant 1, mRNA [NM_031942]
A_23_P144835	ESM1	−2.30845	3.08E−06	3.14E−05	3.14E−05	Down	Homo sapiens endothelial cell-specific molecule 1 (ESM1), mRNA [NM_007036]
A_23_P97283	PAQR6	−0.89962	3.32E−06	3.34E−05	3.34E−05	Down	Homo sapiens progestin and adipoQ receptor family member VI (PAQR6), transcript variant 1, mRNA [NM_024897]
A_23_P58604	MRNIP	−1.12795	3.32E−06	3.34E−05	3.34E−05	Down	MRN complex interacting protein
A_23_P257704	HSPB1	−1.10506	3.58E−06	3.57E−05	3.57E−05	Down	Homo sapiens heat shock 27 kDa protein 1 (HSPB1), mRNA [NM_001540]
A_23_P373119	HMG4L	−1.18587	3.88E−06	3.82E−05	3.82E−05	Down	Homo sapiens high-mobility group (nonhistone chromosomal) protein 4-like (HMG4L) on chromosome 20 [NR_002165]
A_23_P359540	HIST1H4F	−0.98355	3.92E−06	3.85E−05	3.85E−05	Down	Homo sapiens histone 1, H4f (HIST1H4F), mRNA [NM_003540]
A_23_P366216	HIST1H2BH	−1.18347	3.94E−06	3.87E−05	3.87E−05	Down	Homo sapiens histone 1, H2bh (HIST1H2BH), mRNA [NM_003524]
A_23_P213527	GPR150	−1.10403	3.97E−06	3.89E−05	3.89E−05	Down	G protein-coupled receptor 150
A_23_P160518	TRIM45	−1.11378	3.98E−06	3.9E−05	3.9E−05	Down	Homo sapiens tripartite motif-containing 45 (TRIM45), mRNA [NM_025188]
A_23_P92222	MUC20	−0.91405	3.98E−06	3.9E−05	3.9E−05	Down	Homo sapiens mucin 20 (MUC20), mRNA [NM_152673]
A_23_P30813	HIST1H4K	−1.20662	4.04E−06	3.94E−05	3.94E−05	Down	Homo sapiens histone 1, H4k (HIST1H4K), mRNA [NM_003541]
A_23_P134835	ChGn	−1.54034	4.48E−06	4.32E−05	4.32E−05	Down	Homo sapiens chondroitin beta1,4 *N*-acetylgalactosaminyltransferase (ChGn), mRNA [NM_018371]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P12363	ROR1	−1.1345	4.57E−06	4.4E−05	4.4E−05	Down	Homo sapiens receptor tyrosine kinase-like orphan receptor 1 (ROR1), mRNA [NM_005012]
A_23_P403898	PTPN3	−1.01953	4.98E−06	4.74E−05	4.74E−05	Down	Homo sapiens protein tyrosine phosphatase, non-receptor type 3 (PTPN3), mRNA [NM_002829]
A_23_P401718	CCDC74A	−1.80857	5.72E−06	5.36E−05	5.36E−05	Down	Coiled-coil domain containing 74A
A_23_P87742	HOM-TES-103	−1.0777	5.73E−06	5.36E−05	5.36E−05	Down	Homo sapiens HOM-TES-103 tumor antigen-like (HOM-TES-103), transcript variant 2, mRNA [NM_080730]
A_23_P16976	ANXA4	−1.2867	5.87E−06	5.48E−05	5.48E−05	Down	Homo sapiens annexin A4 (ANXA4), mRNA [NM_001153]
A_23_P421664	CAP2	−1.13484	6.53E−06	6.02E−05	6.02E−05	Down	Homo sapiens CAP, adenylatecyclase-associated protein, 2 (yeast) (CAP2), mRNA [NM_006366]
A_23_P323685	HIST1H4H	−0.96637	7.13E−06	6.5E−05	6.5E−05	Down	Homo sapiens histone 1, H4 h (HIST1H4H), mRNA [NM_003543]
A_23_P58706	SPINK5L3	−2.0278	7.14E−06	6.51E−05	6.51E−05	Down	Homo sapiens cDNA FLJ10658 fis, clone NT2RP2006052. [AK001520]
A_23_P112341	C9orf76	−1.04746	7.21E−06	6.56E−05	6.56E−05	Down	Homo sapiens chromosome 9 open reading frame 76 (C9orf76), mRNA [NM_024945]
A_23_P115785	FANK1	−0.9667	7.45E−06	6.71E−05	6.71E−05	Down	Homo sapiens fibronectin type 3 and ankyrin repeat domains 1 (FANK1), mRNA [NM_145235]
A_23_P24716	HSPA5BP1	−1.43386	7.74E−06	6.94E−05	6.94E−05	Down	Homo sapiens heat shock 70 kDa protein 5 (glucose-regulated protein, 78 kDa) binding protein 1 (HSPA5BP1), transcript variant 1, mRNA [NM_017870]
A_23_P30275	PCYOX1L	−1.14979	8.11E−06	7.23E−05	7.23E−05	Down	Prenylcysteine oxidase 1 like
A_23_P59069	HIST1H2BO	−1.1306	8.18E−06	7.28E−05	7.28E−05	Down	Homo sapiens histone 1, H2bo (HIST1H2BO), mRNA [NM_003527]
A_23_P12204	AMY2A	−1.05071	8.52E−06	7.53E−05	7.53E−05	Down	Homo sapiens amylase, alpha 2A; pancreatic (AMY2A), mRNA [NM_000699]
A_23_P200792	NOTCH2	−0.92532	8.58E−06	7.58E−05	7.58E−05	Down	Homo sapiens Notch homolog 2 (Drosophila) (NOTCH2), mRNA [NM_024408]
A_23_P387471	MICB	−0.99885	9.12E−06	7.97E−05	7.97E−05	Down	Homo sapiens MHC class I polypeptide-related sequence B (MICB), mRNA [NM_005931]
A_23_P42908	FLJ90586	−1.15885	9.32E−06	8.12E−05	8.12E−05	Down	Homo sapiens hypothetical protein FLJ90586 (FLJ90586), mRNA [NM_153345]
A_23_P41634	ANKRA2	−1.18157	9.54E−06	8.29E−05	8.29E−05	Down	Homo sapiens ankyrin repeat, family A (RFXANK-like), 2 (ANKRA2), mRNA [NM_023039]
A_23_P35871	E2F8	−1.08092	1.04E−05	8.92E−05	8.92E−05	Down	E2F transcription factor 8
A_23_P348169	MGC35169	−1.01136	1.12E−05	9.59E−05	9.59E−05	Down	Homo sapiens hypothetical protein MGC35169 (MGC35169), mRNA [NM_152324]
A_23_P209241	THC2093007	−1.12635	1.13E−05	9.64E−05	9.64E−05	Down	Unknown
A_23_P377284	TGFA	−1.69157	1.16E−05	9.83E−05	9.83E−05	Down	Homo sapiens transforming growth factor, alpha (TGFA), mRNA [NM_003236]
A_23_P19532	DEF6	−1.13455	1.19E−05	0.000101	0.000101	Down	Homo sapiens differentially expressed in FDCP 6 homolog (mouse) (DEF6), mRNA [NM_022047]
A_23_P204469	PLA2G1B	−1.43416	1.2E−05	0.000101	0.000101	Down	Homo sapiens phospholipase A2, group IB (pancreas) (PLA2G1B), mRNA [NM_000928]
A_23_P34375	TCEA3	−1.15472	1.25E−05	0.000105	0.000105	Down	Homo sapiens transcription elongation factor A (SII), 3 (TCEA3), mRNA [NM_003196]
A_23_P258862	PDCD4	−1.02229	1.32E−05	0.00011	0.00011	Down	Homo sapiens programmed cell death 4 (neoplastic transformation inhibitor) (PDCD4), transcript variant 2, mRNA [NM_145341]
A_23_P167256	PHF17	−1.00459	1.39E−05	0.000115	0.000115	Down	Homo sapiens cDNA: FLJ22479 fis, clone HRC10831. [AK026132]
A_23_P133445	GZMA	−1.46757	1.45E−05	0.000119	0.000119	Down	Homo sapiens granzyme A (granzyme 1, cytotoxic T-lymphocyte-associated serine esterase 3) (GZMA), mRNA [NM_006144]
A_23_P205746	EML1	−1.02566	1.45E−05	0.00012	0.00012	Down	Homo sapiens echinoderm microtubule-associated protein-like 1 (EML1), transcript variant 2, mRNA [NM_004434]
A_23_P145694	ASNS	−0.92634	1.45E−05	0.00012	0.00012	Down	Homo sapiens asparagine synthetase (ASNS), transcript variant 2, mRNA [NM_001673]
A_23_P205273	PPP1R13B	−1.08114	1.48E−05	0.000121	0.000121	Down	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 13B (PPP1R13B), mRNA [NM_015316]
A_23_P37704	CDT1	−1.08028	1.57E−05	0.000127	0.000127	Down	Homo sapiens DNA replication factor (CDT1), mRNA [NM_030928]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P358917	CYP3A7	− 1.904	1.62E−05	0.000131	0.000131	Down	Homo sapiens cytochrome P450, family 3, subfamily A, polypeptide 7 (CYP3A7), mRNA [NM_000765]
A_23_P93180	HIST1H2BC	− 1.04644	1.71E−05	0.000137	0.000137	Down	Homo sapiens histone 1, H2bc (HIST1H2BC), mRNA [NM_003526]
A_23_P157245	MGC9712	− 1.71604	1.77E−05	0.000141	0.000141	Down	Homo sapiens hypothetical protein MGC9712 (MGC9712), mRNA [NM_152689]
A_23_P110122	CCNG2	− 0.91007	1.98E−05	0.000156	0.000156	Down	Homo sapiens cyclin G2 (CCNG2), mRNA [NM_004354]
A_23_P35006	AMY2B	− 1.00577	2.02E−05	0.000158	0.000158	Down	Homo sapiens amylase, alpha 2B; pancreatic (AMY2B), mRNA [NM_020978]
A_23_P50517	ZNF541	− 1.12079	2.13E−05	0.000165	0.000165	Down	Homo sapiens zinc finger protein 541 (ZNF541), mRNA [NM_032255]
A_23_P168427	MGC2463	− 0.97197	2.32E−05	0.000178	0.000178	Down	Homo sapiens hypothetical protein MGC2463 (MGC2463), mRNA [NM_024070]
A_23_P42178	HIST1H2BF	− 1.21743	2.41E−05	0.000184	0.000184	Down	Homo sapiens histone 1, H2bf (HIST1H2BF), mRNA [NM_003522]
A_23_P22422	PNMA3	− 1.01471	2.49E−05	0.000189	0.000189	Down	Homo sapiens paraneoplastic antigen MA3 (PNMA3), mRNA [NM_013364]
A_23_P161076	CD2	− 1.12531	2.49E−05	0.000189	0.000189	Down	Homo sapiens CD2 antigen (p50), sheep red blood cell receptor (CD2), mRNA [NM_001767]
A_23_P111042	HIST1H2BI	− 1.16591	2.65E−05	0.000199	0.000199	Down	Homo sapiens histone 1, H2bi (HIST1H2BI), mRNA [NM_003525]
A_23_P49499	ST6GALNAC2	− 0.92414	2.67E−05	0.000201	0.000201	Down	Homo sapiens sialyltransferase 7 ((alpha-*N*-acetylneuraminyl-2,3-beta-galactosyl-1,3)-*N*-acetyl galactosaminide alpha-2,6-sialyltransferase) B (SIAT7B), mRNA [NM_006456]
A_23_P407565	CX3CR1	− 1.45951	2.7E−05	0.000203	0.000203	Down	Homo sapiens chemokine (C-X3-C motif) receptor 1 (CX3CR1), mRNA [NM_001337]
A_23_P108823	OSBPL6	− 1.53589	2.74E−05	0.000205	0.000205	Down	Homo sapiens oxysterol binding protein-like 6 (OSBPL6), transcript variant 2, mRNA [NM_145739]
A_23_P170587	SMYD2	− 0.90957	3.09E−05	0.000226	0.000226	Down	Homo sapiens SET and MYND domain containing 2 (SMYD2), mRNA [NM_020197]
A_23_P80048	FER1L4	− 1.03432	3.19E−05	0.000233	0.000233	Down	Homo sapiens cDNA FLJ13459 fis, clone PLACE1003366, weakly similar to Homo sapiens otoferlin (OTOF) mRNA. [AK023521]
A_23_P129204	IDH2	− 1.08205	3.22E−05	0.000235	0.000235	Down	Homo sapiens isocitrate dehydrogenase 2 (NADP+), mitochondrial (IDH2), mRNA [NM_002168]
A_23_P21260	U96396	− 1.06605	3.29E−05	0.000238	0.000238	Down	Homo sapiens anti-streptococcal/anti-myosin immunoglobulin kappa light chain variable region mRNA, partial cds. [U96396]
A_23_P30776	HIST1H2BE	− 1.15494	3.32E−05	0.00024	0.00024	Down	Homo sapiens histone 1, H2be (HIST1H2BE), mRNA [NM_003523]
A_23_P8807	CYP3A5	− 2.10112	3.62E−05	0.000259	0.000259	Down	Homo sapiens cytochrome P450, family 3, subfamily A, polypeptide 5 (CYP3A5), mRNA [NM_000777]
A_23_P90510	C19orf32	− 0.93105	3.74E−05	0.000267	0.000267	Down	Homo sapiens chromosome 19 open reading frame 32 (C19orf32), mRNA [NM_138393]
A_23_P40174	MMP9	− 1.02612	3.81E−05	0.000271	0.000271	Down	Homo sapiens matrix metalloproteinase 9 (gelatinase B, 92 kDa gelatinase, 92 kDa type IV collagenase) (MMP9), mRNA [NM_004994]
A_23_P207521	COL1A1	− 2.32625	3.84E−05	0.000273	0.000273	Down	Homo sapiens collagen, type I, alpha 1 (COL1A1), mRNA [NM_000088]
A_23_P135184	RALGDS	− 1.03709	3.87E−05	0.000274	0.000274	Down	Homo sapiens ral guanine nucleotide dissociation stimulator (RALGDS), mRNA [NM_006266]
A_23_P330581	MGC14816	− 1.6498	3.91E−05	0.000277	0.000277	Down	Homo sapiens hypothetical protein MGC14816 (MGC14816), mRNA [NM_144620]
A_23_P325040	TMPO	− 1.05487	3.97E−05	0.000281	0.000281	Down	Homo sapiens thymopoietin (TMPO), mRNA [NM_003276]
A_23_P134204	NYD-SP18	− 1.04885	4.07E−05	0.000286	0.000286	Down	Homo sapiens testes development-related NYD-SP18 (NYD-SP18), mRNA [NM_032599]
A_23_P112531	EEIG1	− 0.90434	4.12E−05	0.000289	0.000289	Down	Homo sapiens early estrogen-induced gene 1 protein (EEIG1), mRNA [NM_203305]
A_23_P93348	LTB	− 1.26861	4.4E−05	0.000306	0.000306	Down	Homo sapiens lymphotoxin beta (TNF superfamily, member 3) (LTB), transcript variant 1, mRNA [NM_002341]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P110253	KIT	− 1.03965	4.51E−05	0.000312	0.000312	Down	Homo sapiens v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog (KIT), mRNA [NM_000222]
A_23_P82814	FBXO32	− 0.9212	4.54E−05	0.000314	0.000314	Down	Homo sapiens F-box protein 32 (FBXO32), transcript variant 1, mRNA [NM_058229]
A_23_P167168	IGJ	− 1.20231	4.65E−05	0.000321	0.000321	Down	Homo sapiens immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides (IGJ), mRNA [NM_144646]
A_23_P253002	IQGAP2	− 0.91408	4.95E−05	0.000338	0.000338	Down	Homo sapiens IQ motif-containing GTPase activating protein 2 (IQGAP2), mRNA [NM_006633]
A_23_P20423	RHOBTB2	− 0.98386	4.96E−05	0.000338	0.000338	Down	Homo sapiens Rho-related BTB domain containing 2 (RHOBTB2), mRNA [NM_015178]
A_23_P503042	F11R	− 0.89175	5.26E−05	0.000356	0.000356	Down	Homo sapiens F11 receptor (F11R), transcript variant 4, mRNA [NM_144503]
A_23_P302672	DDIT4L	− 1.09949	5.37E−05	0.000363	0.000363	Down	Homo sapiens DNA-damage-inducible transcript 4-like (DDIT4L), mRNA [NM_145244]
A_23_P203833	HRB2	− 1.46125	5.55E−05	0.000373	0.000373	Down	Human clone A9A2BRB2 (CAC)n/(GTG)n repeat-containing mRNA. [U00943]
A_23_P126075	KCNK1	− 1.36437	5.9E−05	0.000392	0.000392	Down	Homo sapiens potassium channel, subfamily K, member 1 (KCNK1), mRNA [NM_002245]
A_23_P257516	MICA	− 1.0773	5.92E−05	0.000393	0.000393	Down	Homo sapiens MHC class I polypeptide-related sequence A (MICA), mRNA [NM_000247]
A_23_P389281	HOXA13	− 1.23737	6.21E−05	0.00041	0.00041	Down	Homo sapiens homeo box A13 (HOXA13), mRNA [NM_000522]
A_23_P210763	JAG1	− 1.21052	6.26E−05	0.000412	0.000412	Down	Homo sapiens jagged 1 (Alagille syndrome) (JAG1), mRNA [NM_000214]
A_23_P209179	#N/A	− 1.19543	6.74E−05	0.000439	0.000439	Down	Unknown
A_23_P120594	ACAS2L	− 1.40394	6.86E−05	0.000445	0.000445	Down	Homo sapiens acetyl-Coenzyme A synthetase 2 (AMP forming)-like (ACAS2L), nuclear gene encoding mitochondrial protein, mRNA [NM_032501]
A_23_P69586	FAT	− 0.94498	6.89E−05	0.000446	0.000446	Down	Homo sapiens FAT tumor suppressor homolog 1 (Drosophila) (FAT), mRNA [NM_005245]
A_23_P134764	LY6D	− 0.97294	6.92E−05	0.000447	0.000447	Down	Homo sapiens lymphocyte antigen 6 complex, locus D (LY6D), mRNA [NM_003695]
A_23_P385126	DEPDC7	− 1.00485	7.08E−05	0.000456	0.000456	Down	DEP domain containing 7
A_23_P97700	TXNIP	− 0.95226	7.51E−05	0.00048	0.00048	Down	Homo sapiens thioredoxin interacting protein (TXNIP), mRNA [NM_006472]
A_23_P208880	UHRF1	− 1.03377	7.66E−05	0.000488	0.000488	Down	Homo sapiens ubiquitin-like, containing PHD and RING finger domains, 1 (UHRF1), mRNA [NM_013282]
A_23_P18452	CXCL9	− 1.32349	7.74E−05	0.000492	0.000492	Down	Homo sapiens chemokine (C-X-C motif) ligand 9 (CXCL9), mRNA [NM_002416]
A_23_P7642	SPARC	− 1.3748	8.28E−05	0.00052	0.00052	Down	Homo sapiens secreted protein, acidic, cysteine-rich (osteonectin) (SPARC), mRNA [NM_003118]
A_23_P57779	CLDN1	− 1.56165	8.45E−05	0.00053	0.00053	Down	Homo sapiens claudin 1 (CLDN1), mRNA [NM_021101]
A_23_P82449	DFNA5	− 1.46031	9.32E−05	0.000579	0.000579	Down	Homo sapiens deafness, autosomal dominant 5 (DFNA5), mRNA [NM_004403]
A_23_P92710	RHOBTB3	− 1.12791	9.35E−05	0.00058	0.00058	Down	Homo sapiens Rho-related BTB domain containing 3 (RHOBTB3), mRNA [NM_014899]
A_23_P434398	C6orf198	− 1.46965	9.38E−05	0.000582	0.000582	Down	Homo sapiens mRNA; cDNA DKFZp451F022 (from clone DKFZp451F022); complete cds. [AL834248]
A_23_P218523	C19orf28	− 0.96389	9.86E−05	0.000606	0.000606	Down	Homo sapiens clone PP3501 unknown mRNA. [AF218008]
A_23_P47034	HHEX	− 1.09146	0.000102	0.000621	0.000621	Down	Homo sapiens hematopoietically expressed homeobox (HHEX), mRNA [NM_002729]
A_23_P422851	CABLES1	− 0.899	0.000103	0.000628	0.000628	Down	Homo sapiens Cdk5 and Abl enzyme–substrate 1 (CABLES1), mRNA [NM_138375]
A_23_P215566	AHR	− 0.98237	0.000106	0.000644	0.000644	Down	Homo sapiens aryl hydrocarbon receptor (AHR), mRNA [NM_001621]
A_23_P52610	DDB2	− 1.16576	0.000107	0.000652	0.000652	Down	Homo sapiens damage-specific DNA binding protein 2, 48 kDa (DDB2), mRNA [NM_000107]
A_23_P134910	GGH	− 1.24449	0.000108	0.000654	0.000654	Down	Homo sapiens gamma-glutamyl hydrolase (conjugase, folylpolygammaglutamyl hydrolase) (GGH), mRNA [NM_003878]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P19379	HIST1H2BD	− 1.04573	0.000117	0.000701	0.000701	Down	Homo sapiens histone 1, H2bd (HIST1H2BD), transcript variant 1, mRNA [NM_021063]
A_23_P40470	H2BFS	− 0.92793	0.000118	0.000706	0.000706	Down	Homo sapiens H2B histone family, member S (H2BFS), mRNA [NM_017445]
A_23_P94380	C9orf58	− 1.82609	0.000118	0.000706	0.000706	Down	Homo sapiens chromosome 9 open reading frame 58 (C9orf58), transcript variant 1, mRNA [NM_031426]
A_23_P93260	PRSS16	− 0.99751	0.000126	0.000748	0.000748	Down	Homo sapiens protease, serine, 16 (thymus) (PRSS16), mRNA [NM_005865]
A_23_P259692	PSAT1	− 1.24735	0.000126	0.000749	0.000749	Down	Homo sapiens phosphoserine aminotransferase 1 (PSAT1), transcript variant 1, mRNA [NM_058179]
A_23_P96115	HLA-DQB1	− 0.99689	0.000128	0.000757	0.000757	Down	Human MHC class II HLA-DQ-beta (DR2-DQw1/DR4 DQw3) mRNA, complete cds, clone ROF2D. [M20432]
A_23_P158096	COL27A1	− 1.19008	0.000152	0.000877	0.000877	Down	Homo sapiens cDNA FLJ11895 fis, clone HEMBA1007301, weakly similar to COLLAGEN ALPHA 1(III) CHAIN. [AK021957]
A_23_P154605	SULF2	− 1.72829	0.00017	0.000966	0.000966	Down	Homo sapiens sulfatase 2 (SULF2), transcript variant 1, mRNA [NM_018837]
A_23_P120902	LGALS2	− 0.91718	0.000172	0.000976	0.000976	Down	Homo sapiens lectin, galactoside-binding, soluble, 2 (galectin 2) (LGALS2), mRNA [NM_006498]
A_23_P133851	HIST1H2BJ	− 1.14485	0.000193	0.001075	0.001075	Down	Homo sapiens histone 1, H2bj (HIST1H2BJ), mRNA [NM_021058]
A_23_P207999	PMAIP1	− 1.09713	0.000199	0.001105	0.001105	Down	Homo sapiens phorbol-12-myristate-13-acetate-induced protein 1 (PMAIP1), mRNA [NM_021127]
A_23_P20864	ANGPTL2	− 0.95258	0.000201	0.001114	0.001114	Down	Homo sapiens angiopoietin-like 2 (ANGPTL2), mRNA [NM_012098]
A_23_P138985	CD3D	− 1.0322	0.000209	0.001155	0.001155	Down	Homo sapiens CD3D antigen, delta polypeptide (TiT3 complex) (CD3D), mRNA [NM_000732]
A_23_P91850	IL20RB	− 1.29946	0.000223	0.001224	0.001224	Down	Interleukin 20 receptor subunit beta
A_23_P204170	TMPO	− 1.0423	0.000228	0.001244	0.001244	Down	HSU09086 thymopoietin alpha {Homo sapiens;}, partial (16%) [THC2199856]
A_23_P211141	DSCAM	− 1.15284	0.000234	0.001274	0.001274	Down	Homo sapiens Down syndrome cell adhesion molecule (DSCAM), transcript variant 1, mRNA [NM_001389]
A_23_P111054	HIST1H2BB	− 0.98191	0.000258	0.001388	0.001388	Down	Homo sapiens histone 1, H2bb (HIST1H2BB), mRNA [NM_021062]
A_23_P333029	ERICH5	− 1.24862	0.00026	0.001396	0.001396	Down	Glutamate rich 5
A_23_P21912	LOC58489	− 0.93044	0.000262	0.001406	0.001406	Down	Homo sapiens hypothetical protein from EUROIMAGE 588495, mRNA (cDNA clone IMAGE:30346383), partial cds. [BC059401]
A_23_P206884	BE769278	− 1.28597	0.000265	0.001419	0.001419	Down	BE769278 PM4-FT0027-050600-001-a03 FT0027 Homo sapiens cDNA, mRNA sequence [BE769278]
A_23_P163467	CCDC9B	− 1.07659	0.000282	0.001496	0.001496	Down	Coiled-coil domain containing 9B
A_23_P39885	DPP4	− 1.39059	0.000294	0.001547	0.001547	Down	Homo sapiens dipeptidylpeptidase 4 (CD26, adenosine deaminasecomplexing protein 2) (DPP4), mRNA [NM_001935]
A_23_P393051	TMPO	− 0.9548	0.000306	0.001603	0.001603	Down	Homo sapiens hypothetical protein FLJ34633 (FLJ34633), mRNA [NM_152365]
A_23_P216361	COL14A1	− 1.11932	0.000306	0.001603	0.001603	Down	Homo sapiens collagen, type XIV, alpha 1 (undulin) (COL14A1), mRNA [NM_021110]
A_23_P83736	ING1L	− 0.95405	0.000322	0.001675	0.001675	Down	Homo sapiens inhibitor of growth family, member 1-like (ING1L), mRNA [NM_001564]
A_23_P251662	SMS	− 0.89441	0.000359	0.001836	0.001836	Down	Homo sapiens spermine synthase (SMS), mRNA [NM_004595]
A_23_P165968	SEMG1	− 1.24063	0.000363	0.001857	0.001857	Down	Homo sapiens semenogelin I (SEMG1), transcript variant 1, mRNA [NM_003007]
A_23_P142527	COL3A1	− 1.84985	0.000403	0.002035	0.002035	Down	Homo sapiens collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant) (COL3A1), mRNA [NM_000090]
A_23_P158817	AF272774	− 1.81668	0.000424	0.00212	0.00212	Down	Homo sapiens factor VII active site mutant immunoconjugate mRNA, complete cds. [AF272774]
A_23_P162668	CPM	− 1.00539	0.000424	0.002122	0.002122	Down	Homo sapiens carboxypeptidase M (CPM), transcript variant 1, mRNA [NM_001874]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P42407	HLA-DRB4	− 0.94276	0.000438	0.002176	0.002176	Down	Homo sapiens major histocompatibility complex, class II, DR beta 4 (HLA-DRB4), mRNA [NM_021983]
A_23_P217797	DDX3Y	− 1.15954	0.00047	0.002315	0.002315	Down	Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, Y-linked (DDX3Y), mRNA [NM_004660]
A_23_P140884	TUBB7P	− 1.02291	0.000514	0.002494	0.002494	Down	Tubulin beta 7 pseudogene
A_23_P23664	PALMD	− 0.92556	0.00052	0.002514	0.002514	Down	Homo sapiens palmdelphin (PALMD), mRNA [NM_017734]
A_23_P24674	OR8U1	− 0.95413	0.000546	0.002622	0.002622	Down	Homo sapiens olfactory receptor, family 8, subfamily U, member 1 (OR8U1), mRNA [NM_001005204]
A_23_P106925	CHST6	− 1.33851	0.0006	0.002849	0.002849	Down	Homo sapiens carbohydrate (*N*-acetylglucosamine 6-*O*) sulfotransferase 6 (CHST6), mRNA [NM_021615]
A_23_P116183	BCDO2	− 1.32876	0.000625	0.002944	0.002944	Down	Homo sapiens beta-carotene dioxygenase 2 (BCDO2), mRNA [NM_031938]
A_23_P87879	CD69	− 1.00474	0.000636	0.002988	0.002988	Down	Homo sapiens CD69 antigen (p60, early T-cell activation antigen) (CD69), mRNA [NM_001781]
A_23_P56746	FAP	− 1.67165	0.000664	0.003099	0.003099	Down	Homo sapiens fibroblast activation protein, alpha (FAP), mRNA [NM_004460]
A_23_P8571	SRCRB4D	− 1.14765	0.000691	0.003203	0.003203	Down	Homo sapiens scavenger receptor cysteine-rich domain containing, group B (4 domains) (SRCRB4D), mRNA [NM_080744]
A_23_P148088	FGG	− 2.84226	0.000693	0.003206	0.003206	Down	Homo sapiens fibrinogen, gamma polypeptide (FGG), transcript variant gamma-B, mRNA [NM_021870]
A_23_P205111	POSTN	− 1.63912	0.000716	0.0033	0.0033	Down	Homo sapiens periostin, osteoblast specific factor (POSTN), mRNA [NM_006475]
A_23_P392384	C9orf58	− 1.43472	0.000792	0.003583	0.003583	Down	Homo sapiens chromosome 9 open reading frame 58 (C9orf58), transcript variant 1, mRNA [NM_031426]
A_23_P59470	BC038972	− 1.04069	0.00083	0.003735	0.003735	Down	Homo sapiens, Similar to hypothetical protein, MNCb-3350, clone IMAGE:5216914, mRNA. [BC038972]
A_23_P60599	UGT1A6	− 1.1118	0.000929	0.004095	0.004095	Down	Homo sapiens UDP glycosyltransferase 1 family, polypeptide A6 (UGT1A6), transcript variant 1, mRNA [NM_001072]
A_23_P108676	FLJ13391	− 0.97197	0.000941	0.004139	0.004139	Down	Homo sapiens hypothetical protein FLJ13391 (FLJ13391), mRNA [NM_032181]
A_23_P102058	MATN3	− 0.99367	0.000984	0.004292	0.004292	Down	Homo sapiens matrilin 3 (MATN3), mRNA [NM_002381]
A_23_P73632	NR0B1	− 1.74574	0.001026	0.004451	0.004451	Down	Homo sapiens nuclear receptor subfamily 0, group B, member 1 (NR0B1), mRNA [NM_000475]
A_23_P81898	UBD	− 1.68476	0.001105	0.004724	0.004724	Down	Homo sapiens ubiquitin D (UBD), mRNA [NM_006398]
A_23_P54546	TPSAB1	− 0.92143	0.001136	0.004841	0.004841	Down	Homo sapiens tryptase alpha/beta 1 (TPSAB1), mRNA [NM_003294]
A_23_P23996	MAT1A	− 1.26278	0.001202	0.00508	0.00508	Down	Homo sapiens methionine adenosyltransferase I, alpha (MAT1A), mRNA [NM_000429]
A_23_P74012	SPRR1A	− 1.20188	0.001253	0.005261	0.005261	Down	Homo sapiens small proline-rich protein 1A (SPRR1A), mRNA [NM_005987]
A_23_P103703	HSPB7	− 0.91414	0.001398	0.005774	0.005774	Down	Homo sapiens heat shock 27 kDa protein family, member 7 (cardiovascular) (HSPB7), mRNA [NM_014424]
A_23_P320242	KIAA1324L	− 0.95068	0.001415	0.005835	0.005835	Down	KIAA1324 like
A_23_P120819	IGLL1	− 0.94769	0.001489	0.006082	0.006082	Down	Homo sapiens immunoglobulin lambda-like polypeptide 1 (IGLL1), transcript variant 1, mRNA [NM_020070]
A_23_P128918	LGALS3	− 0.97597	0.001518	0.006179	0.006179	Down	Homo sapiens lectin, galactoside-binding, soluble, 3 (galectin 3) (LGALS3), mRNA [NM_002306]
A_23_P137478	THC2046518	− 0.89665	0.001578	0.006382	0.006382	Down	SP2E_HUMAN (P22531) Small proline-rich protein 2E (SPR-2E) (Small proline-rich protein II) (SPR-II), complete [THC2046518]
A_23_P218128	IGHM	− 1.42676	0.001882	0.007361	0.007361	Down	Homo sapiens immunoglobulin heavy constant mu, mRNA (cDNA clone MGC:52291 IMAGE:4765763), complete cds. [BC041037]
A_23_P30254	PLK2	− 0.94795	0.001971	0.007642	0.007642	Down	Homo sapiens polo-like kinase 2 (Drosophila) (PLK2), mRNA [NM_006622]
A_23_P41917	HOMER1	− 0.94646	0.002063	0.007914	0.007914	Down	Homo sapiens homer homolog 1 (Drosophila) (HOMER1), mRNA [NM_004272]
A_23_P82651	NPTX2	− 1.73965	0.002416	0.008984	0.008984	Down	Homo sapiens neuronal pentraxin II (NPTX2), mRNA [NM_002523]

Table 1 (continued)

Agiliant Id	Gene symbol	LogFC	*P* value	FDR	*T* value	Regulation	Gene name
A_23_P91669	PIB5PA	− 0.90311	0.002428	0.009013	0.009013	Down	Homo sapiens phosphatidylinositol (4,5) bisphosphate 5-phosphatase, A (PIB5PA), transcript variant 1, mRNA [NM_014422]
A_23_P25194	HRK	− 1.17507	0.002459	0.009098	0.009098	Down	Homo sapiens harakiri, BCL2 interacting protein (contains only BH3 domain) (HRK), mRNA [NM_003806]
A_23_P60848	AB064167	− 1.11106	0.002565	0.009423	0.009423	Down	Homo sapiens IGL mRNA for immunoglobulin lambda light chain VLJ region, partial cds, clone:L27. [AB064167]
A_23_P84060	HNT	− 0.93816	0.002791	0.01009	0.01009	Down	Homo sapiens neurotrimin (HNT), mRNA [NM_016522]
A_23_P23221	GADD45A	− 1.07302	0.003307	0.011544	0.011544	Down	Homo sapiens growth arrest and DNA-damage-inducible, alpha (GADD45A), mRNA [NM_001924]
A_23_P16254	KLK1	− 1.4422	0.003395	0.0118	0.0118	Down	Homo sapiens kallikrein 1, renal/pancreas/salivary (KLK1), mRNA [NM_002257]
A_23_P259314	RPS4Y1	− 2.41445	0.003589	0.01234	0.01234	Down	Homo sapiens ribosomal protein S4, Y-linked 1 (RPS4Y1), mRNA [NM_001008]
A_23_P435390	#N/A	− 0.89835	0.003607	0.012391	0.012391	Down	Unknown
A_23_P154526	GRB14	− 1.0291	0.003697	0.012625	0.012625	Down	Homo sapiens growth factor receptor-bound protein 14 (GRB14), mRNA [NM_004490]
A_23_P123853	CCL19	− 1.08999	0.003703	0.012642	0.012642	Down	Homo sapiens chemokine (C–C motif) ligand 19 (CCL19), mRNA [NM_006274]
A_23_P209925	FN1	− 1.12765	0.003842	0.013037	0.013037	Down	Homo sapiens fibronectin 1 (FN1), transcript variant 3, mRNA [NM_002026]
A_23_P324384	RPS4Y2	− 2.03269	0.004344	0.014369	0.014369	Down	Homo sapiens ribosomal protein S4, Y-linked 2 (RPS4Y2), mRNA [NM_138963]
A_23_P34518	FABP3	− 0.9477	0.005523	0.017475	0.017475	Down	Homo sapiens fatty acid-binding protein 3, muscle and heart (mammary-derived growth inhibitor) (FABP3), mRNA [NM_004102]
A_23_P206359	CDH1	− 1.47406	0.005541	0.017528	0.017528	Down	Homo sapiens cadherin 1, type 1, E-cadherin (epithelial) (CDH1), mRNA [NM_004360]
A_23_P8175	PLAGL1	− 1.24388	0.006657	0.020448	0.020448	Down	Homo sapiens pleiomorphic adenoma gene-like 1 (PLAGL1), transcript variant 1, mRNA [NM_002656]
A_23_P91230	SLPI	− 1.54692	0.006957	0.021183	0.021183	Down	Homo sapiens secretory leukocyte protease inhibitor (anti-leukoproteinase) (SLPI), mRNA [NM_003064]
A_23_P67381	SULT2A1	− 1.32934	0.007208	0.021769	0.021769	Down	Homo sapiens sulfotransferase family, cytosolic, 2A, dehydroepiandrosterone (DHEA)-preferring, member 1 (SULT2A1), mRNA [NM_003167]
A_23_P33196	COL5A2	− 0.89184	0.007608	0.022696	0.022696	Down	Homo sapiens collagen, type V, alpha 2 (COL5A2), mRNA [NM_000393]
A_23_P122445	HIST1H1C	− 1.19428	0.007795	0.023122	0.023122	Down	Homo sapiens histone 1, H1c (HIST1H1C), mRNA [NM_005319]
A_23_P133862	C6orf194	− 0.96503	0.008225	0.024067	0.024067	Down	Homo sapiens chromosome 6 open reading frame 194 (C6orf194), mRNA [NM_001007531]
A_23_P170713	#N/A	− 1.10382	0.00912	0.026141	0.026141	Down	Unknown
A_23_P162916	SERPINA3	− 1.39724	0.009986	0.028155	0.028155	Down	Homo sapiens serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3 (SERPINA3), mRNA [NM_001085]
A_23_P136724	NMRAL2P	− 0.99278	0.010484	0.029233	0.029233	Down	NmrA like redox sensor 2, pseudogene
A_23_P169437	LCN2	− 0.91733	0.013882	0.036461	0.036461	Down	Homo sapiens lipocalin 2 (oncogene 24p3) (LCN2), mRNA [NM_005564]
A_23_P340088	PRSS8	− 0.89366	0.014299	0.037306	0.037306	Down	Homo sapiens protease, serine, 8 (prostasin) (PRSS8), mRNA [NM_002773]
A_23_P259065	PDE8B	− 0.9067	0.01545	0.039755	0.039755	Down	Homo sapiens phosphodiesterase 8B (PDE8B), mRNA [NM_003719]
A_23_P34345	VCAM1	− 1.14333	0.016486	0.041988	0.041988	Down	Homo sapiens vascular cell adhesion molecule 1 (VCAM1), transcript variant 1, mRNA [NM_001078]
A_23_P25030	RODH	− 1.30011	0.016947	0.042978	0.042978	Down	Homo sapiens 3-hydroxysteroid epimerase (RODH), mRNA [NM_003725]
A_23_P69171	SUCNR1	− 1.07545	0.016987	0.043048	0.043048	Down	Homo sapiens succinate receptor 1 (SUCNR1), mRNA [NM_033050]

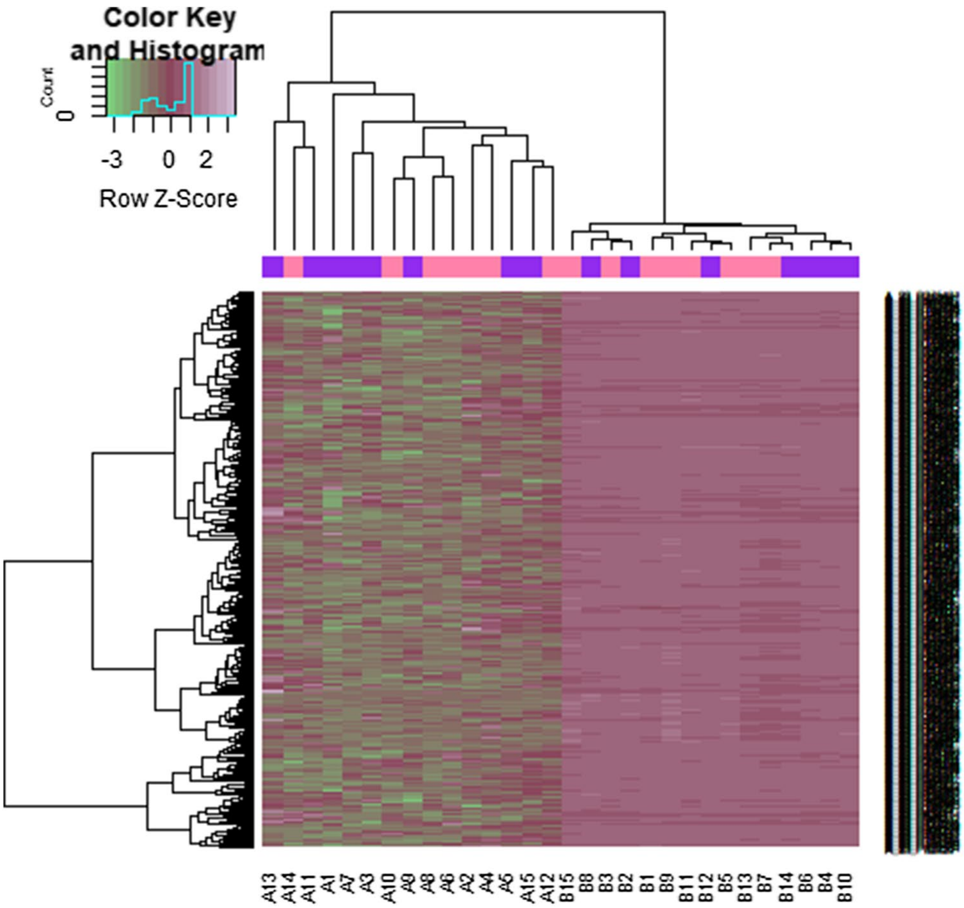
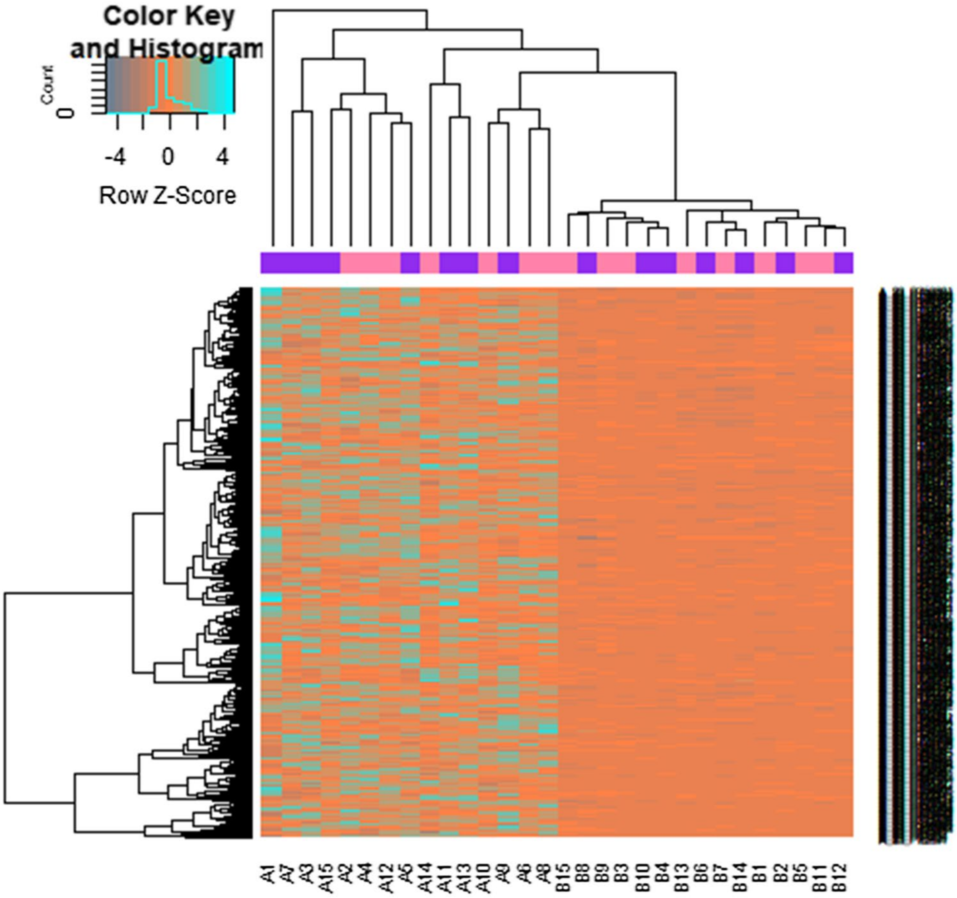


Fig. 3 Heat map of gene expression (Upregulated genes). The color key represents the logFC of DEGs. FC, fold change (A1,A2, A3, A4, A5, A6, A7, A8, A9,A10, A11, A12, A13, A14, A15 = adrenocortical carcinoma samples, B1,B2, B3, B4, B5,B6, B7, B8, B9,B10, B11, B12, B13, B14, B15 = normal whole adrenal gland samples)

PPI network and sub-modules analysis

We constructed a PPI network to further explore the interaction between the common DEGs (up and down regulated) by using PINA database and Cytoscape. A total of 5050 nodes and 9534 edges were included in the PPI networks (up regulated) (Fig. 5). The hub genes with highest node degree in this PPI network such as YWHAZ (degree = 805), HSPA5 (degree = 394), STAT3 (degree = 213), APOE (degree = 183), and GRK5 (degree = 175) are listed in Table 6. A total of 5146 nodes and 11,499 edges were included in the PPI networks (down regulated) (Fig. 6). The hub genes with highest node degree in this PPI network such as FN1 (degree = 1012), VCAM1 (degree = 671), UBD (degree = 664), BARD1 (degree = 252), and TK1 (degree = 169) are listed in Table 6. R square = 0.761 and correlation coefficient = 0.967 for node degree (up regulated) (Fig. 7a), meanwhile *R* square = 0.761 and correlation coefficient = 0.978 for node degree (down regulated) (Fig. 7b). The hub genes with highest betweenness in PPI network for up regulated genes such as YWHAZ (betweenness = 0.26018915), HSPA5 (betweenness = 0.10211544), STAT3 (betweenness = 0.05179592), TH (betweenness = 0.05146886), and CD83 (betweenness = 0.04395976) are listed in Table 6. *R* square = 0.602 and correlation coefficient = 0.105 for betweenness (Fig. 8a). The hub genes with highest stress in PPI network for up regulated genes such as YWHAZ (stress = 110811588), HSPA5 (stress = 43035116), ICAM1 (stress = 27529814), HOXB2 (stress = 23,027,092), and STAT3 (stress = 22,678,172) are listed in Table 6. *R* square = 0.001 and correlation coefficient = 0.111 for stress (Fig. 8b). The hub genes with highest closeness in PPI network for up regulated genes such as YWHAZ (closeness = 0.40211725), HSPA5 (closeness = 0.38225204), NR4A1 (closeness = 0.36144752), IRS1 (closeness = 0.35719883), and MAP3K5 (closeness = 0.35502372) are listed in Table 6. *R* square = 0.186 and correlation coefficient = 0.338 for closeness (Fig. 8c). The hub genes with lowest clustering coefficient in PPI network for up regulated genes such as CRLF1 (clustering coefficient = 0), CRH (clustering coefficient = 0), ARHGAP18 (clustering coefficient = 0), FJX1 (clustering coefficient = 0), and FMO3 (clustering coefficient = 0) are listed in Table 6. R square = 0.447 and correlation coefficient = 0.686 for clustering coefficient (Fig. 8d). The hub genes with highest betweenness in PPI network for down regulated genes such as FN1 (betweenness = 0.24710836), UBD (betweenness = 0.14892195), VCAM1 (betweenness = 0.11467148),

Fig. 4 Heat map of gene expression (Down-regulated genes). The color key represents the logFC of DEGs. FC, fold change (A1,A2, A3, A4, A5, A6, A7, A8, A9,A10, A11, A12, A13, A14, A15 = adrenocortical carcinoma samples, B1,B2, B3, B4, B5,B6, B7, B8, B9,B10, B11, B12, B13, B14, B15 = normal whole adrenal gland samples)



BARD1 (betweenness = 0.05118512), and TK1 (betweenness = 0.04488624) are listed in Table 6. *R* square = 0.574 and correlation coefficient = 0.109 for betweenness (Fig. 9a). The hub genes with highest stress in PPI network for down regulated genes such as FN1 (stress = 358,695,218), UBD (stress = 286,343,980), VCAM1 (stress = 222,971,648), SLPI (stress = 46,566,718), and BARD1 (stress = 43,410,948) are listed in Table 6. *R* square = 0.011 and correlation coefficient = 0.090 for stress (Fig. 9b). The hub genes with highest closeness in PPI network for down regulated genes such as FN1 (closeness = 0.42073523), VCAM1 (closeness = 0.39252408), MCM3 (closeness = 0.39092723), PHGDH (closeness = 0.38138386), and MCM6 (closeness = 0.3806143) are listed in Table 6. *R* square = 0.198 and correlation coefficient = 0.293 for closeness (Fig. 9c). The hub genes with lowest clustering coefficient in PPI network for down regulated genes such as CYP3A5 (clustering coefficient = 0), POPDC2 (clustering coefficient = 0), PNLIPRP2 (clustering coefficient = 0), KIAA1407 (clustering coefficient = 0), and CX3CR1 (clustering coefficient = 0) are listed in Table 6. *R* square = 0.663 and correlation coefficient = 0.810 for clustering coefficient (Fig. 9d).

Subsequently, we performed module analysis of the whole network by the PEWCC1 plug-in. A total of 773 modules were obtained from the PPI network (up regulated). The four most significant modules were selected in this PPI network such as module 6, module 30, module 37, and module 55 (Fig. 10). Module 6 had 48 nodes and 119 edges. Hub genes in this modules such as YWHAZ (degree = 805), GRK5 (degree = 175), and NOLC1 (degree = 99). Module 30 had 10 nodes and 19 edges. Hub genes in this modules such as ID2 (degree = 46), STAT3 (degree = 213), HES1 (degree = 43), NR4A1 (degree = 116), ZNF331 (degree = 11), and YWHAZ (degree = 805). Module 37 had 8 nodes and 22 edges. Hub genes in this modules such as APOE (degree = 183), PLAT (degree = 34), C1S (degree = 12), SERPING1 (degree = 137), HP (degree = 160), APOC1 (degree = 151), and SH3BP5 (degree = 142). Module 55 had 7 nodes and 12 edges. Hub genes in this modules such as STAT1 (degree = 174), IPO7 (degree = 47), and HSPA4L (degree = 40). Meanwhile, total of 923 modules were obtained from the PPI network (down regulated). The four most significant modules were selected in this PPI network such as module 2, module 8, module 10, and module 27 (Fig. 11). Module 2 had 69 nodes and 239 edges. Hub genes in this modules such as VCAM1 (degree = 671), FN1 (degree = 1012), MCM3 (degree = 126), MCM2 (degree = 110), and MCM6

Table 2 The enriched pathway terms of the upregulated differentially-expressed genes

Pathway ID	Pathway name	LogP	Gene count	Genes
BIOCYC				
142238	Catecholamine biosynthesis	3.329361677	02	DDC,PNMT
545304	Glucocorticoid biosynthesis	2.867928265	02	CYP17A1,CYP21A2
545305	Mineralocorticoid biosynthesis	2.867928265	02	CYP11B2,CYP21A2
907943	Superpathway of steroid hormone biosynthesis	2.730759796	03	CYP11B2,CYP17A1,CYP21A2
545352	Acetone degradation I (to methylglyoxal)	1.928835991	02	ADH1B,AKR1B1
545295	Retinoate biosynthesis I	1.928835991	02	ALDH1A1,ALDH1A3
545354	Noradrenaline and adrenaline degradation	1.825833565	02	ADH1B,PNMT
142437	Nicotine degradation IV	1.735054511	02	AOX1,FMO3
142427	Sulfate activation for sulfonation	1.37218863	01	PAPSS2
142362	Lysine degradation I (saccharopine pathway)	1.37218863	01	AASS
545298	Thyroid hormone biosynthesis	1.37218863	01	CTSD
KEGG				
1272485	Aldosterone synthesis and secretion	10	12	CYP11A1,CYP11B2,CYP21A2,HSD3B1,HSD3B2,KCNK3,LDLR,MC2R,NR4A1,NR4A2,PRKD3,SCARB1
82959	Tyrosine metabolism	10	10	ADH1A,ADH1B,ADH1C,ALDH1A3,AOC3,AOX1,DBH,DDC,PNMT,TH
413357	Catecholamine biosynthesis, tyrosine => dopamine => noradrenaline => adrenaline	5.992618886	04	DBH,DDC,PNMT,TH
212237	Mineral absorption	5.935400699	09	ATP1B3,HEPH,MT1A,MT1B,MT1E,MT1F,MT1G,MT1H,MT1X
83032	Drug metabolism—cytochrome P450	5.653260441	10	ADH1A,ADH1B,ADH1C,ALDH1A3,AOX1,FMO2,FMO3,GSTA4,GSTT2,MGST1
413396	Steroid hormone biosynthesis, cholesterol =>prognenolone => progesterone	5.001251815	03	CYP11A1,HSD3B1,HSD3B2
413383	C19/C18-Steroid hormone biosynthesis, pregnenolone =>androstenedione =>estrone	4.415617071	03	CYP17A1,HSD3B1,HSD3B2
790011	Ovarian steroidogenesis	4.057663675	07	CYP11A1,CYP17A1,HSD3B1,HSD3B2,LDLR,PLA2G4A,SCARB1
413395	C21-Steroid hormone biosynthesis, progesterone => cortisol/cortisone	3.730605412	03	CYP11B2,CYP17A1,CYP21A2
812256	TNF signaling pathway	3.287936973	09	CCL2,CEBPB,CXCL1,CXCL2,ICAM1,IL6,JUNB,MAP3K5,SOCS3
83093	Adipocytokinesignaling pathway	1.792970322	05	IRS1,NPY,PCK1,SOCS3,STAT3
Pathway interaction database				
137932	IL6-mediated signaling events	4.493424802	07	CEBPB,CEBPD,IL6,JUNB,SOCS3,STAT1,STAT3
138000	IL23-mediated signaling events	3.912645481	06	CCL2,CXCL1,IL6,SOCS3,STAT1,STAT3
138006	ATF-2 transcription factor network	3.789436765	07	DUSP5,HES1,IL6,JUNB,PDGFRA,SOCS3,TH
169349	Validated transcriptional targets of AP1 family members Fra1 and Fra2	3.136325106	05	CCL2,DCN,GJA1,IL6,JUNB
138045	HIF-1-alpha transcription factor network	1.896922132	05	ABCB1,ADM,CXCL12,ID2,NDRG1
137911	FOXA2 and FOXA3 transcription factor networks	1.84366283	04	ALAS1,CEBPB,CEBPD,PCK1

Table 2 (continued)

Pathway ID	Pathway name	LogP	Gene count	Genes
137929	IL27-mediated signaling events	1.754112281	03	IL6,STAT1,STAT3
137945	amb2 Integrin signaling	1.716046245	04	HP,ICAM1,IL6,PLAT
138017	Signaling events mediated by PTP1B	1.657185008	04	CDH2,IRS1,SOCS3,STAT3
137976	IL2-mediated signaling events	1.601261646	04	IRS1,SOCS3,STAT1,STAT3
138020	Class I PI3K signaling events mediated by Akt	1.446218048	03	CASP9,MAP3K5,YWHAZ
REACTOME				
1339158	Metallothioneins bind metals	10	07	MT1A,MT1B,MT1E,MT1F,MT1G,MT1H,MT1X
1270046	Metabolism of steroid hormones	10	09	AKR1B1,CYP11A1,CYP11B2,CYP17A1,CYP21A2,FDX1,HSD3B1,HSD3B2,STARD6
1339157	Response to metal ions	10	07	MT1A,MT1B,MT1E,MT1F,MT1G,MT1H,MT1X
1270190	Phase 1—functionalization of compounds	10	15	AADAC,ADH1A,ADH1B,ADH1C,ALDH1A1,AOC3,CYP11A1,CYP11B2,CYP17A1,CYP21A2,CYP26B1,CYP4B1,FDX1,FMO2,FMO3
1270189	Biological oxidations	10	23	AADAC,ADH1A,ADH1B,ADH1C,ALDH1A1,AOC3,AS3MT,CYP11A1,CYP11B2,CYP17A1,CYP21A2,CYP26B1,CYP4B1,FDX1,FMO2,FMO3,GCLM,GSTA4,GSTT2,MAT2A,MGST1,PAPSS2,TPMT
1270176	Catecholamine biosynthesis	10	04	DBH,DDC,PNMT,TH
1270048	Glucocorticoid biosynthesis	10	05	CYP11B2,CYP17A1,CYP21A2,HSD3B1,HSD3B2
1270049	Mineralocorticoid biosynthesis	5.522938037	04	CYP11B2,CYP21A2,HSD3B1,HSD3B2
1270047	Pregnenolone biosynthesis	4.40636003	04	AKR1B1,CYP11A1,FDX1,STARD6
1269325	Interleukin-6 signaling	4.217440473	04	IL6,SOCS3,STAT1,STAT3
1269318	Signaling by Interleukins	2.615336	22	CCL2,CEBPD,CRLF1,CXCL1,CXCL2,DUSP16,DUSP5,FGF23,FGF7,FGF9,ICAM1,IL1R2,IL1RL1,IL6,IRS1,JUNB,PDGFRA,SAA1,SOCS3,STAT1,STAT3,YWHAZ
GenMAPP				
MAP00140	Steroid hormone metabolism	10	06	CYP11A1,CYP11B2,CYP17A1,CYP21A2,HSD3B1,HSD3B2
MAP00350	Tyrosine metabolism	10	10	ADH1A,ADH1B,ADH1C,ALDH1A3,AOC3,AOX1,DBH,DDC,PNMT,TH
MAP00561	Glycerolipid metabolism	5.211990421	08	ADH1A,ADH1B,ADH1C,AKR1B1,ALDH1A1,ALDH3A2,GK,PLA2G4A
MAP00120	Bile acid biosynthesis	5.165492191	06	ADH1A,ADH1B,ADH1C,ALDH1A1,ALDH3A2,SOAT1
MAP00340	Histidine metabolism	4.283791459	05	ALDH1A1,ALDH1A3,ALDH3A2,AOC3,DDC
MAP00380	Tryptophan metabolism	3.377500876	06	ALDH1A1,ALDH3A2,AOC3,AOX1,CYP4B1,DDC
MAP00071	Fatty acid metabolism	3.377500876	06	ADH1A,ADH1B,ADH1C,ALDH1A1,ALDH3A2,CYP4B1
MAP00620	Pyruvate metabolism	3.327781725	05	AKR1B1,ALDH1A1,ALDH3A2,PC,PCK1
MAP00010	Glycolysis Gluconeogenesis	3.086924749	06	ADH1A,ADH1B,ADH1C,ALDH1A1,ALDH1A3,ALDH3A2
MAP00310	Lysine degradation	2.352545877	03	AASS,ALDH1A1,ALDH3A2
MAP00480	Glutathione metabolism	1.954315707	03	GCLM,GSTT2,MGST1

Table 2 (continued)

Pathway ID	Pathway name	LogP	Gene count	Genes
MSigDB C2 BIOCARTA (v6.0)				
M5889	Ensemble of genes encoding extracellular matrix and extracellular matrix-associated proteins	4.119278713	41	ADAMTS1,ADAMTS9,ANGPTL1,ANGPTL4,CCL13,CCL2,CCN3,CRLF1,CTSD,CXCL1,CXCL12,CXCL2,DCN,EFEMP1,FBLN1,FBLN5,FCN2,FGF12,FGF23,FGF7,FGF9,FMOD,GDF15,IGFBP2,IGFBP5,IGFBP6,IL6,LUM,MFAP4,PLAT,S100A8,S100A9,SEMA3B,SEMA6A,SERPING1,SPOCK3,SPON2,SRPX2,THBS1,TIMP4,TNXB
M4557	Biosynthesis of neurotransmitters	3.730605412	03	DBH,PNMT,TH
M5884	Ensemble of genes encoding core extracellular matrix including ECM glycoproteins, collagens and proteoglycans	3.533619686	16	CCN3,DCN,EFEMP1,FBLN1,FBLN5,FMOD,IGFBP2,IGFBP5,IGFBP6,LUM,MFAP4,SPOCK3,SPON2,SRPX2,THBS1,TNXB
M3008	Genes encoding structural ECM glycoproteins	2.970975905	12	CCN3,EFEMP1,FBLN1,FBLN5,IGFBP2,IGFBP5,IGFBP6,MFAP4,SPON2,SRPX2,THBS1,TNXB
M18899	Repression of pain sensation by the transcriptional regulator DREAM	2.525871625	03	CREM,PRKAR1A,PRKAR2B
M5883	Genes encoding secreted soluble factors	2.50991094	16	ANGPTL1,ANGPTL4,CCL13,CCL2,CRLF1,CXCL1,CXCL12,CXCL2,FGF12,FGF23,FGF7,FGF9,GDF15,IL6,S100A8,S100A9
M8066	IL22 soluble receptor signaling pathway	2.352545877	03	SOCS3,STAT1,STAT3
M1394	GATA3 participate in activating the Th2 cytokine genes expression	2.352545877	03	JUNB,PRKAR1A,PRKAR2B
M6778	IL-10 anti-inflammatory signaling pathway	2.275094252	03	IL6,STAT1,STAT3
M3952	Cells and molecules involved in local acute inflammatory response	2.275094252	03	C7,ICAM1,IL6
M5885	Ensemble of genes encoding ECM-associated proteins including ECM-affilaited proteins, ECM regulators and secreted factors	1.704959721	25	ADAMTS1,ADAMTS9,ANGPTL1,ANGPTL4,CCL13,CCL2,CRLF1,CTSD,CXCL1,CXCL12,CXCL2,FCN2,FGF12,FGF23,FGF7,FGF9,GDF15,IL6,PLAT,S100A8,S100A9,SEMA3B,SEMA6A,SERPING1,TIMP4
PantherDB				
P05912	Dopamine receptor mediated signaling pathway	3.946608731	07	DBH,DDC,EPB41L1,GNAZ,KCNK3,PRKAR2B,TH
P00001	Adrenaline and noradrenaline biosynthesis	3.542737228	05	DBH,DDC,PNMT,SLC18A1,TH
P06587	Nicotine pharmacodynamics pathway	3.46815455	05	CHRNA3,DDC,EPB41L1,KCNK3,TH
P04372	5-Hydroxytryptamine degredation	2.20277477	03	ALDH1A1,ALDH1A3,ALDH3A2
P02772	Pyruvate metabolism	2.047621635	02	PC,PCK1
P00046	Oxidative stress response	1.778106454	04	DUSP16,DUSP5,PLA2G4A,STAT1
P00018	EGF receptor signaling pathway	1.492499822	06	MAP3K5,MRAS,PRKD3,STAT1,STAT3,YWHAZ
P05913	Enkephalin release	1.479597446	03	CREM,PENK,PRKAR2B
P02778	Sulfate assimilation	1.37218863	01	PAPSS2
P00005	Angiogenesis	1.368776963	07	CASP9,DLL1,PDGFRA,PLA2G4A,PRKD3,STAT1,STAT3
P00039	Metabotropic glutamate receptor group III pathway	1.316122901	04	GRIK1,PRKAR1A,PRKAR2B,SLC1A2
Pathway ontology				
PW:0000363	Leptin system	4.04871932	04	IRS1,NPY,SOCS3,STAT3
PW:0000238	Insulin-like growth factor signaling	4.04871932	04	IGFBP2,IGFBP5,IGFBP6,IRS1
PW:0000052	Tyrosine metabolic	3.512683309	04	ALDH3A2,AOX1,DDC,TH

Table 2 (continued)

Pathway ID	Pathway name	LogP	Gene count	Genes
PW:0000018	Parkinson disease	3.512683309	04	CASP9,NR4A2,TH,UCHL1
PW:0000166	Nicotinate and nicotinamidemetabolic	2.730759796	03	AOX1,CD38,TESK1
PW:0000482	Lipoprotein metabolic	2.6237154	03	APOC1,APOE,SCARB1
PW:0000043	Pyruvate metabolic	2.437279868	04	AKR1B1,ALDH3A2,PC,PDK4
PW:0000484	Altered lipoprotein metabolic	2.047621635	02	APOC1,APOE
PW:0000133	Selenoamino acid metabolic	1.928835991	02	CTH,MAT2A
PW:0000054	Tryptophan metabolic	1.900441706	02	ALDH3A2,AOX1,DDC
PW:0000016	Amyotrophic lateral sclerosis disease	1.397565099	02	NEFH,SLC1A2
SMPDB				
SMP00012	Catecholamine biosynthesis	10	04	DBH,DDC,PNMT,TH
SMP00130	Steroidogenesis	4.86871625	04	CYP11A1,CYP17A1,CYP21A2,HSD3B1
SMP00006	Tyrosine metabolism	3.876318671	05	ADH1A,DBH,DDC,PNMT,TH
SMP00307	Propranolol pathway	3.403522613	04	DBH,DDC,PRKAR1A,TH
SMP00299	Betaxolol pathway	3.403522613	04	DBH,DDC,PRKAR1A,TH
SMP00196	Leigh syndrome	2.20277477	03	AKR1B1,PC,PCK1
SMP00060	Pyruvate metabolism	2.20277477	03	AKR1B1,PC,PCK1
SMP00068	Androgen and estrogen metabolism	1.825833565	02	CYP17A1,HSD3B1
SMP00013	Cysteine metabolism	1.825833565	02	CTH,GCLM
SMP00029	Selenoamino acid metabolism	1.825833565	02	CTH,MAT2A
SMP00375	Verapamil pathway	1.472855807	04	ATP1B3,CALD1,EDNRB,KCNQ1

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

Pathway ID	Pathway name	LogP	Gene count	Genes
BIOCYC				
782392	Pyrimidine deoxyribonucleosides salvage	2.43427714	02	TK1,TYMS
142235	Glutamate removal from folates	1.699047736	01	GGH
142290	Spermine biosynthesis	1.699047736	01	SMS
547505	Oxidized GTP and dGTP detoxification	1.699047736	01	NUDT1
782381	Pyrimidine deoxyribonucleotides biosynthesis from CTP	1.469058982	02	RRM2,TYMS
782380	Pyrimidine deoxyribonucleotides de novo biosynthesis	1.469058982	02	RRM2,TYMS
782391	Superpathway of pyrimidine deoxyribonucleoside salvage	1.416613253	02	TK1,TYMS
1108787	Protein *O*-[*N*-acetyl]-glucosylation	1.410922427	01	OGT
142134	Asparagine biosynthesis	1.410922427	01	ASNS
142191	GDP-L-fucose biosynthesis II (from L-fucose)	1.410922427	01	FUK
1108783	Purine deoxyribonucleosides degradation	1.410922427	01	ADA
KEGG				
83122	Systemic lupus erythematosus	10	17	HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HLA-DQB1,HLA-DRB4
658418	Viral carcinogenesis	10	17	CCNE1,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,PMAIP1
585563	Alcoholism	10	16	GRIN2C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K
83055	p53 signaling pathway	10	10	BBC3,CCNB1,CCNB2,CCNE1,CCNG2,DDB2,GADD45A,IGFBP3,PMAIP1,RRM2
83045	Mismatch repair	5.390718967	06	EXO1,LIG1,MSH2,POLD1,RFC4,RFC5
83039	DNA replication	5.280926757	07	LIG1,MCM2,MCM3,MCM6,POLD1,RFC4,RFC5
83054	Cell cycle	4.501851947	11	BUB1,CCNB1,CCNB2,CCNE1,GADD45A,MAD2L1,MCM2,MCM3,MCM6,PTTG1,TTK
413353	Methionine degradation	2.961765192	03	DNMT1,DNMT3B,MAT1A
413350	Serine biosynthesis, glycerate-3P => serine	2.945794549	02	PHGDH,PSAT1
172847	Protein digestion and absorption	2.718264551	07	COL14A1,COL1A1,COL27A1,COL3A1,COL4A5,COL5A2,DPP4
1404797	Platinum drug resistance	1.849235095	05	BBC3,BIRC5,MSH2,PMAIP1,TOP2A
Pathway interaction database				
137935	FOXM1 transcription factor network	5.197100329	07	BIRC5,CCNB1,CCNB2,CENPF,NEK2,TGFA,XRCC1
137934	E2F transcription factor network	4.060732898	08	CCNE1,MCM3,MYBL2,RRM2,SULT2A1,TK1,TYMS,XRCC1
137959	BARD1 signaling events	3.649167392	05	BARD1,CCNE1,FANCA,FANCG,RAD51
137939	Direct p53 effectors	3.57205794	10	BBC3,CCNB1,DDB2,GADD45A,IGFBP3,MSH2,PMAIP1,PPP1R13B,TGFA,TP53INP1

Table 3 (continued)

BIOCYC				
Pathway ID	Pathway name	LogP	Gene count	Genes
169351	Validated targets of C-MYC transcriptional activation	2.293998874	06	BIRC5,CCNB1,CDCA7,MMP9,PMAIP1,TK1
137972	Signaling events mediated by HDAC Class III	2.160334014	04	HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K
138080	Aurora B signaling	2.160334014	04	BIRC5,BUB1,CDCA8,RACGAP1
138054	Nectin adhesion pathway	1.905235291	03	CDH1,CLDN1,F11R
138064	Syndecan-4-mediated signaling events	1.651447862	03	FN1,LAMA3,MMP9
137925	Aurora A signaling	1.651447862	03	BIRC5,GADD45A,TPX2
138062	Signaling events mediated by HDAC Class II	1.545705979	03	ANKRA2,NCOR2,NR3C1
REACTOME				
1269738	SIRT1 negatively regulates rRNA Expression	10	16	HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,TAF1C
1269734	Epigenetic regulation of gene expression	10	20	DNMT1,DNMT3B,EZH2,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,TAF1C,UHRF1
1269855	Deposition of new CENPA-containing nucleosomes at the centromere	10	16	HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,OIP5
1269856	Telomere maintenance	10	19	HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,LIG1,POLD1,RFC4,RFC5
1339139	Activation of HOX genes during differentiation	10	17	EZH2,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,NCOA6
1269737	Negative epigenetic regulation of rRNA expression	10	18	DNMT1,DNMT3B,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4-J,HIST1H4K,TAF1C
1269864	Packaging of telomere ends	10	15	HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K
1269723	Transcriptional regulation by small RNAs	10	16	HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,NUP107
1269659	RNA polymerase I promoter opening	10	15	HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K

Table 3 (continued)

Pathway ID	Pathway name	LogP	Gene count	Genes
BIOCYC				
1269741	Cell cycle	10	54	BARD1,BIRC5,BUB1,CCNB1,CCNB2,CCNE1,CDCA5,CDCA8,CDT1,CENPF,CEP192,EXO1,GMNN,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HMMR,KIF18A,KNTC1,LIG1,MAD2L1,MCM2,MCM3,MCM6,MCM8,MYBL2,NEK2,NUP107,OIP5,POLD1,PTTG1,RAD51,RFC4,RFC5,RRM2,SPC25,STAG3,TMPO,TOP2A,TPX2,TYMS,ZWINT
1269650	Generic transcription pathway	4.720695561	36	BARD1,BBC3,BIRC5,CCNB1,CCNE1,DDB2,DYRK2,EXO1,GADD45A,IGFBP3,KIT,MAPKAPK5,MSH2,MYBL2,NCOA6,NCOR2,NOTCH2,NR0B1,NR3C1,PLAGL1,PLK2,PMAIP1,PPP1R13B,PPP1R13L,RFC4,RFC5,SMYD2,TGFA,TP53INP1,TPX2,ZNF133,ZNF266,ZNF302,ZNF443,ZNF606,ZNF700
GenMAPP				
MAP00271	Methionine metabolism	2.004006898	02	DNMT1,MAT1A
MAP00240	Pyrimidine metabolism	1.97569821	04	POLD1,RRM2,TK1,TYMS
MAP00790	Folate biosynthesis	1.65400981	02	GGH,TYMS
MSigDB C2 BIOCARTA				
M6682	CDK regulation of DNA replication	4.714442339	05	CCNE1,CDT1,MCM2,MCM3,MCM6
M5884	Ensemble of genes encoding core extracellular matrix including ECM glycoproteins, collagens and proteoglycans	3.981813788	16	COL14A1,COL1A1,COL27A1,COL3A1,COL4A5,COL5A2,ESM1,FGG,FN1,IGFBP3,LAMA3,LAMB1,MATN3,NTN4,POSTN,SPARC
M3005	Genes encoding collagen proteins	3.69561031	06	COL14A1,COL1A1,COL27A1,COL3A1,COL4A5,COL5A2
M5889	Ensemble of genes encoding extracellular matrix and extracellular matrix-associated proteins	2.483967022	33	ANGPT2,ANGPTL2,ANXA4,CCL19,COL14A1,COL1A1,COL27A1,COL3A1,COL4A5,COL5A2,CXCL9,ESM1,FGG,FN1,IGFBP3,LAMA3,LAMB1,LGALS2,LGALS3,LTB,MATN3,MMP28,MMP9,MUC20,NTN4,PLXDC1,POSTN,SERPINA3,SLPI,SPARC,SULF2,TGFA,WNT5A
M16966	Stathmin and breast cancer resistance to antimicrotubule agents	2.243196398	03	CCNB1,CD2,CD3D
M5887	Genes encoding structural components of basement membranes	2.121178927	04	COL4A5,LAMA3,LAMB1,NTN4
M3008	Genes encoding structural ECM glycoproteins	1.818444608	09	FGG,FN1,IGFBP3,LAMA3,LAMB1,MATN3,NTN4,POSTN,SPARC
M7239	Apoptotic DNA fragmentation and tissue homeostasis	1.809165229	02	HMGB2,TOP2A
M3075	Granzyme A mediated apoptosis pathway	1.727607669	02	GZMA,HMGB2
M12012	p38 MAPK pathway	1.450737606	03	GADD45A,HSPB1,MAPKAPK5
PantherDB				
P00034	Integrin signaling pathway	2.776571831	10	COL14A1,COL1A1,COL27A1,COL3A1,COL4A5,COL5A2,FN1,LAMA3,LAMB1,NTN4
P02776	Serine glycine biosynthesis	2.43427714	02	PHGDH,PSAT1
P00059	p53 pathway	2.34726807	06	CCNB1,CCNE1,DDB2,GADD45A,IGFBP3,RRM2

Table 3 (continued)

BIOCYC				
Pathway ID	Pathway name	LogP	Gene count	Genes
P00004	Alzheimer disease-presenilin pathway	1.625403066	06	CDH1,FZD6,MMP28,MMP9,NOTCH2,WNT5A
P02739	De novo pyrimidine deoxyribonucleotide biosynthesis	1.52565134	02	RRM2,TYMS
P00045	Notch signaling pathway	1.450737606	03	JAG1,NCOR2,NOTCH2
P00017	DNA replication	1.416613253	02	POLD1,TOP2A
P02759	Pyridoxal-5-phosphate biosynthesis	1.410922427	01	PSAT1
P00050	Plasminogen activating cascade	1.367792454	02	FGG,MMP9
Pathway ontology				
PW:0000662	Mismatch repair pathway	5.054073891	06	EXO1,LIG1,MSH2,POLD1,RFC4,RFC5
PW:0000130	Nucleotide excision repair	3.408612225	02	LIG1,POLD1
PW:0000088	G1/S transition	2.945794549	02	CCNB1,CCNE1
PW:0000129	Base excision repair	2.650477895	02	LIG1,XRCC1
PW:0000104	Intrinsic apoptotic	2.63352124	04	BBC3,BMF,HRK,PMAIP1
PW:0000349	Alagille syndrome	1.699047736	01	JAG1
PW:0000157	Glycosaminoglycan metabolic	1.699047736	01	GUSB
PW:0000095	G1/S DNA-damage checkpoint	1.699047736	01	CCNE1
PW:0000189	Folate mediated one-carbon metabolic	1.469058982	02	GGH,TYMS
PW:0000091	G2/M transition	1.410922427	01	CCNB1
PW:0000299	Myocardial infarction	1.410922427	01	LGALS2
SMPDB				
SMP00144	Adenosine deaminase deficiency	1.699047736	01	ADA

Table 4 The enriched GO terms of the upregulated differentially-expressed genes

GO ID	CATEGORY	GO name	LogP	Gene count	Genes
GO:0048514	BP	Blood vessel morphogenesis	10	38	ADAMTS1,ADM,ANGPTL4,APOE,CCL13,CCL2,CCN3,CDH2,CITED1,CXCL12,DCN,DLL1,ENPP2,FGF9,FZD4,GATA6,GJA1,HAND2,HES1,HOXA5,HOXA7,IL6,JUNB,NR4A1,NRXN3,PDGFRA,RAMP1,SCG2,SIRT1,SRPX2,STARD13,STAT1,TFAP2B,TGFBR3,THBS1,TIPARP,UNC5B,XBP1
GO:0051707	BP	Response to other organism	10	44	ABR,ADM,CASP9,CCL13,CCL2,CEBPB,CHGA,CITED1,CXCL1,CXCL12,CXCL2,CYP17A1,DCN,DNAJC3,EDNRB,FCN2,FGF7,HP,ICAM1,IER3,IL6,JUNB,KCNQ1,LITAF,MGST1,MTSS1,NPY,P2RY2,PDK4,PENK,PLA2G4A,PTGIR,PTX3,S100A8,S100A9,SCARB1,SLC25A19,SOCS3,SPON2,STAT1,TH,TIMP4,TNFRSF11B,XBP1
GO:0043069	BP	Negative regulation of programmed cell death	10	39	ANGPTL4,APOE,CCL2,CD38,CEBPB,CITED1,CRLF1,CTH,CXCL12,DHCR24,DLL1,DNAJC3,EDNRB,GATA6,GCLM,GRK5,HAND2,HSPA1A,HSPA5,ICAM1,IER3,IL6,NR4A1,NR4A2,NR4A3,PDK4,RGN,SCG2,SIRT1,SNAI1,SOCS3,STAT3,TBX3,TFAP2B,TGFBR3,THBS1,UNC5B,XBP1,YWHAZ
GO:0001944	BP	Vasculature development	10	42	ADAMTS1,ADM,ANGPTL4,APOE,CCL13,CCL2,CCN3,CDH2,CITED1,CTH,CXCL12,DCN,DLL1,EGR1,ENPP2,FGF9,FZD4,GATA6,GJA1,HAND2,HES1,HOXA5,HOXA7,IL6,JUNB,NR4A1,NRXN3,PDGFRA,RAMP1,SCG2,SIRT1,SOCS3,SRPX2,STARD13,STAT1,TBX3,TFAP2B,TGFBR3,THBS1,TIPARP,UNC5B,XBP1
GO:0008207	BP	C21-steroid hormone metabolic process	10	08	ADM,AKR1B1,CYP11A1,CYP11B2,CYP17A1,CYP21A2,DKK3,FDX1
GO:0035150	BP	Regulation of tube size	10	15	ADM,ADRA2C,APOE,CD38,CHGA,DBH,EDNRB,GCLM,GJA1,HBB,ICAM1,NPY1R,P2RY2,SIRT1,TGFBR3
GO:0040012	BP	Regulation of locomotion	10	41	ABR,ACVR1C,AOC3,APOE,ARHGAP18,CCL13,CCL2,CCN3,CXCL1,CXCL12,CXCL2,DCN,EFEMP1,EGR1,ENPP2,FBLN1,FGF7,GTPBP4,HOXA7,HSPA5,ICAM1,IGFBP5,IL6,INSM1,IRS1,P2RY2,PDGFRA,PTP4A1,PTX3,RARRES2,RGN,SCARB1,SCG2,SEMA3B,SEMA6A,SNAI1,SRPX2,STARD13,STAT3,TGFBR3,THBS1
GO:0050880	BP	Regulation of blood vessel size	10	15	ADM,ADRA2C,APOE,CD38,CHGA,DBH,EDNRB,GCLM,GJA1,HBB,ICAM1,NPY1R,P2RY2,SIRT1,TGFBR3
GO:0040013	BP	Negative regulation of locomotion	10	19	ABR,ACVR1C,APOE,CCL2,CCN3,CXCL12,DCN,FBLN1,GTPBP4,HOXA7,IGFBP5,PTX3,RGN,SEMA3B,SEMA6A,STARD13,STAT3,TGFBR3,THBS1

Table 4 (continued)

GO ID	CATEGORY	GO name	LogP	Gene count	Genes
GO:0033993	BP	Response to lipid	10	56	ABR,ADAMTS1,ADH1C,ADM,CASP9,CCL13,CCL2,CD38,CEBPB,CITED1,CRH,CXCL1,CXCL2,CYP17A1,CYP26B1,DCN,EDNRB,FGF23,FOSL2,FZD4,GATA6,ICAM1,IGFBP2,IL6,JUNB,LDLR,LITAF,MGST1,NEFH,NPC1,NPY1R,NR2F1,NR4A1,NR4A2,NR4A3,P2RY2,PDK4,PENK,PID1,PLA2G4A,PON1,PTGIR,S100A8,SCARB1,SIRT1,SOCS3,SPON2,STAT1,STAT3,TGFBR3,TH,THBS1,TIMP4,TNFRSF11B,WFDC1,XBP1
GO:0031012	CC	Extracellular matrix	10	24	ADAMTS1,ADAMTS9,ANGPTL4,APOE,CCN3,CTSD,DCN,EFEMP1,FBLN1,FBLN5,FGF9,FMOD,IL1RL1,LUM,MFAP4,PLAT,RARRES2,SPOCK3,SPON2,TGFBR3,THBS1,TIMP4,TNFRSF11B,TNXB
GO:0005615	CC	Extracellular space	10	68	ADAMTS9,ADM,AKR1B1,ANGPTL1,ANGPTL4,AOC3,APOC1,APOE,ATP4A,C1S,CCL13,CCL2,CHGA,CPE,CRH,CRLF1,CTSD,CXCL1,CXCL12,CXCL2,DCN,DKK3,EFEMP1,ENPP2,FBLN1,FBLN5,FCN2,FGF12,FGF23,FGF7,FGF9,FJX1,FMOD,GDF15,HBB,HP,HSPA1A,ICAM1,IGFBP2,IGFBP5,IGFBP6,IL1RL1,IL6,LDLR,LUM,NPY,PI16,PLAT,PON1,PTX3,RAMP1,S100A8,S100A9,SAA1,SCG2,SEMA3B,SERPING1,SPOCK3,SPON2,SRPX2,TGFBR3,THBS1,TIMP4,TNFRSF11B,TNXB,VASN,WFDC1,YWHAZ
GO:0031410	CC	Cytoplasmic vesicle	10	49	ADAMTS1,APOE,ATP1B3,CCL13,CCL2,CD163,CHGA,CHGB,CPE,CTSD,CYB561,DBH,DDC,DLL1,DUSP16,ECE2,FZD4,GABARAPL1,GJA1,HBB,HP,HSPA5,IGFBP2,KCNQ1,LDLR,MARCO,MTSS1,NPTX1,NPY1R,PLA2G4A,PLAT,RAB20,RAB21,RAB34,RAB38,RARRES2,SAA1,SCAP,SCARB1,SCG2,SCG3,SERPING1,SLC18A1,SLC2A3,SYT13,SYT4,TH,THBS1,YWHAZ
GO:0044433	CC	Cytoplasmic vesicle part	10	29	APOE,CD163,CHGA,CPE,DBH,ECE2,FZD4,GABARAPL1,GJA1,HBB,HP,KCNQ1,LDLR,MARCO,RAB20,RAB21,RAB34,RAB38,RARRES2,SAA1,SCAP,SCARB1,SCG3,SERPING1,SLC18A1,SLC2A3,SYT4,TH,THBS1,YWHAZ
GO:0097708	CC	Intracellular vesicle	10	48	ADAMTS1,APOE,ATP1B3,CCL13,CCL2,CD163,CHGA,CHGB,CPE,CTSD,CYB561,DBH,DDC,DLL1,DUSP16,ECE2,FZD4,GABARAPL1,GJA1,HBB,HP,HSPA5,IGFBP2,KCNQ1,LDLR,MARCO,MTSS1,NPTX1,NPY1R,PLA2G4A,PLAT,RAB20,RAB21,RAB34,RAB38,RARRES2,SAA1,SCAP,SCARB1,SCG2,SCG3,SERPING1,SLC18A1,SLC2A3,SYT13,SYT4,TH,THBS1,YWHAZ
GO:0071953	CC	Elastic fiber	4.728300681	03	FBLN1,FBLN5,MFAP4

Table 4 (continued)

GO ID	CATEGORY	GO name	LogP	Gene count	Genes
GO:0030659	CC	Cytoplasmic vesicle membrane	4.665655637	23	CD163,CHGA,CPE,DBH,ECE2,FZD4,GABARAPL1,GJA1,KCNQ1,LDLR,MARCO,RAB20,RAB21,RAB34,RAB38,SCAP,SCARB1,SCG3,SLC18A1,SLC2A3,SYT4,TH,YWHAZ
GO:0098857	CC	Membrane microdomain	4.644464195	18	ATP1B3,CDH2,CPE,CTSD,DLL1,EDNRB,GJA1,GPM6B,ICAM1,IRS1,KCNQ1,LDLR,NPC1,PRKAR1A,PRKAR2B,SCARB1,SLC2A3,UNC5B
GO:0045121	CC	Membrane raft	4.644464195	18	ATP1B3,CDH2,CPE,CTSD,DLL1,EDNRB,GJA1,GPM6B,ICAM1,IRS1,KCNQ1,LDLR,NPC1,PRKAR1A,PRKAR2B,SCARB1,SLC2A3,UNC5B
GO:0030424	CC	Axon	4.442446857	24	ADRA2C,CCL13,CCL2,CCN3,CLDN5,CRH,CYP17A1,DBH,DDC,DLG2,GRIK1,NEFH,NPY,NPY1R,PENK,PNMT,RAB21,SEMA6A,SIRT1,SLC1A2,STAT1,STMN2,TH,UCHL1
GO:0008201	MF	Heparin binding	10	14	ADAMTS1,APOE,CCL13,CCL2,CCN3,FGF12,FGF7,FGF9,FMOD,LXN,SAA1,TGFBR3,THBS1,TNXB
GO:0001664	MF	G protein-coupled receptor binding	10	20	ADM,ADRA2C,CCL13,CCL2,CRH,CXCL1,CXCL12,CXCL2,EDNRB,GNAZ,HSPA1A,MRAP,NPY,P2RY2,PENK,RAMP1,SAA1,STAT1,STAT3,UCHL1
GO:0005539	MF	Glycosaminoglycan binding	10	16	ADAMTS1,APOE,CCL13,CCL2,CCN3,DCN,FGF12,FGF7,FGF9,FMOD,LXN,SAA1,SPOCK3,TGFBR3,THBS1,TNXB
GO:0004497	MF	Monooxygenase activity	10	12	CH25H,CYP11A1,CYP11B2,CYP17A1,CYP21A2,CYP26B1,CYP4B1,DBH,FDX1,FMO2,FMO3,TH
GO:1901681	MF	Sulfur compound binding	5.692974952	17	ADAMTS1,APOE,CCL13,CCL2,CCN3,FGF12,FGF7,FGF9,FMOD,LXN,MGST1,PC,SAA1,SOAT1,TGFBR3,THBS1,TNXB
GO:0000982	MF	Transcription factor activity, RNA polymerase II proximal promoter sequence-specific DNA binding	5.406912331	20	CEBPB,CEBPD,EGR1,FOSL2,FOXK2,HAND2,HES1,HOXA5,HOXA7,INSM1,JUNB,NFIL3,NR4A1,NR4A2,NR4A3,PHOX2B,SNAI1,STAT3,TBX3,TFAP2B
GO:0001047	MF	Core promoter binding	5.38561477	13	CEBPB,CREM,EGR1,GATA6,INSM1,NFIL3,NR4A2,NR4A3,SFPQ,SIRT1,STAT1,TFAP2B,XBP1
GO:0016491	MF	Oxidoreductase activity	4.997417778	30	AASS,ADH1A,ADH1B,ADH1C,AKR1B1,ALDH1A1,ALDH1A3,ALDH3A2,AOC3,AOX1,CH25H,CYB561,CYP11A1,CYP11B2,CYP17A1,CYP21A2,CYP26B1,CYP4B1,DBH,DHCR24,FDX1,FMO2,FMO3,GSTT2,HBB,HEPH,HSD3B1,HSD3B2,MGST1,TH
GO:0035259	MF	Glucocorticoid receptor binding	4.909190407	05	CEBPB,NR4A1,NR4A2,NR4A3,STAT3
GO:0031406	MF	Carboxylic acid-binding	4.855820497	15	APOC1,CYP26B1,DBH,DDC,FMO3,GRIK1,MAT2A,PC,PCK1,S100A8,S100A9,SCARB1,SYT4,TH,THBS1

Table 5 The enriched GO terms of the down-regulated differentially-expressed genes

GO ID	CATEGORY	GO name	LogP	Gene count	Genes
GO:0044770	BP	Cell cycle phase transition	10	30	ANLN,BIRC5,BUB1,CABLES1,CCNB1,CCNB2,CCNE1,CDCA5,CDKN3,CDT1,CENPF,CEP192,EZH2,GADD45A,HMMR,KNTC1,MAD2L1,MCM2,MCM3,MCM6,MCM8,MELK,NEK2,PLAGL1,PLK2,RRM2,TIMELESS,TPX2,TTK,TYMS
GO:0051985	BP	Negative regulation of chromosome segregation	10	08	BUB1,CCNB1,CENPF,CEP192,CHTF18,MAD2L1,PTTG1,TTK
GO:0006323	BP	DNA packaging	10	25	CCNB1,CDCA5,CHAF1A,CHAF1B,H2BFS,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HMGB2,MCM2,OIP5,TOP2A
GO:0007088	BP	Regulation of mitotic nuclear division	10	15	ANLN,BIRC5,BUB1,CCNB1,CDCA5,CENPF,CEP192,HOXA13,KIF11,KNTC1,MAD2L1,NEK2,PTTG1,TGFA,TTK
GO:0034728	BP	Nucleosome organization	10	22	CHAF1A,CHAF1B,H2BFS,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HMGB2,MCM2,OIP5
GO:0072331	BP	Signal transduction by p53 class mediator	10	18	BARD1,BBC3,CCNB1,DYRK2,EXO1,GADD45A,MAPKAPK5,MSH2,PLAGL1,PLK2,PMAIP1,PPP1R13B,PPP1R13L,RFC4,RFC5,SMYD2,TP53INP1,TPX2
GO:0007062	BP	Sister chromatid cohesion	10	13	BIRC5,BUB1,CDCA5,CDCA8,CENPF,KIF18A,KIF22,KNTC1,MAD2L1,NUP107,SPC25,STAG3,ZWINT
GO:0022402	BP	Cell cycle process	10	71	ANLN,ASPM,BARD1,BIRC5,BUB1,CABLES1,CCNB1,CCNB2,CCNE1,CCNG2,CDCA2,CDCA5,CDCA8,CDKN3,CDT1,CENPF,CEP192,CHTF18,CKAP2,E2F8,EML1,EZH2,FANCA,FANCG,FAP,GADD45A,HMMR,HOXA13,KIF11,KIF18A,KIF22,KNTC1,LIG1,MAD2L1,MCM2,MCM3,MCM6,MCM8,MELK,MSH2,MYBL2,NEK2,NEK3,NOTCH2,NR3C1,NUP107,OIP5,PBK,PHGDH,PIMREG,PLAGL1,PLK2,PRC1,PTTG1,RAB11FIP4,RACGAP1,RAD51,RAD54L,RRM2,SPAG5,SPC25,STAG3,TGFA,TIMELESS,TOP2A,TP53INP1,TPX2,TTK,TYMS,WNT5A,ZWINT
GO:0043062	BP	Extracellular structure organization	10	23	CDH1,COL14A1,COL1A1,COL27A1,COL3A1,COL4A5,COL5A2,DDR1,DPP4,F11R,FAP,FGG,FN1,LAMA3,LAMB1,LGALS3,MATN3,MMP9,POSTN,SPARC,SULF2,TPSAB1,VCAM1
GO:0007051	BP	Spindle organization	10	15	ASPM,BIRC5,CCNB1,CEP192,EML1,KIF11,MYBL2,NEK2,PLK2,PRC1,RACGAP1,SPAG5,SPC25,TPX2,TTK

Table 5 (continued)

GO ID	CATEGORY	GO name	LogP	Gene count	Genes
GO:0000775	CC	Chromosome, centromeric region	10	19	BIRC5,BUB1,CCNB1,CDCA5,CDCA8,CENPF,DNMT1,DNMT3B,KIF18A,KIF22,KNTC1,MAD2L1,NEK2,NUP107,OIP5,SPAG5,SPC25,STAG3,ZWINT
GO:0005819	CC	Spindle	10	21	ASPM,BIRC5,CCNB1,CDCA8,CENPF,CKAP2,EML1,HSPB1,KIF11,KIF18A,KIF22,KNTC1,MAD2L1,NEK2,NR3C1,PRC1,RAB11FIP4,RACGAP1,SPAG5,TPX2,TTK
GO:0005615	CC	Extracellular space	10	56	ADA,AMY1A,AMY2A,AMY2B,ANGPT2,ANGPTL2,CCL19,COL14A1,COL1A1,COL3A1,CPM,CXCL9,DDR1,FABP3,FAP,FGG,FN1,GGH,GUSB,H2BFS,HIST1H2BC,HIST1H2BE,HIST1H2BF,HIST1H2BI,HIST1H2BJ,HMGB2,HSPB1,IGFBP3,IGHM,IGLL1,KIT,LAMB1,LCN2,LGALS3,LRIG3,LTB,MICA,MMP9,NUDT1,PLA2G1B,PLXDC1,PNLIPRP2,POSTN,PRSS8,RAB11FIP4,SEMG1,SERPINA3,SLPI,SPARC,STAG3,SULF2,TGFA,TPSAB1,VCAM1,WNT5A,ZG16B
GO:0000785	CC	Chromatin	10	38	BRD8,CDCA5,CENPF,CHAF1A,CHAF1B,DNMT1,DNMT3B,ENC1,EZH2,H2BFS,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HMGB2,IGFBP3,KIF22,MCM2,NCOR2,OGT,OIP5,PLK2,RAD51,TIMELESS,TMPO,UHRF1
GO:0044427	CC	Chromosomal part	10	61	BIRC5,BRD8,BUB1,CCNB1,CDCA5,CDCA8,CENPF,CHAF1A,CHAF1B,CHTF18,DNMT1,DNMT3B,ENC1,EZH2,H2BFS,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HMBOX1,HMGB2,IGFBP3,KIF18A,KIF22,KNTC1,MAD2L1,MCM2,MCM3,MCM6,MSH2,MYBL2,NCOR2,NEK2,NUP107,OGT,OIP5,PLK2,POLD1,RAD51,RFC4,RFC5,SPAG5,SPC25,STAG3,THOC3,TIMELESS,TMPO,UHRF1,ZWINT
GO:0000788	CC	Nuclear nucleosome	10	12	H2BFS,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO

Table 5 (continued)

GO ID	CATEGORY	GO name	LogP	Gene count	Genes
GO:0000228	CC	Nuclear chromosome	10	43	BIRC5,BRD8,BUB1,CCNB1,CDCA5,CHAF1A,CHAF1B,DNMT3B,ENC1,EZH2,H2BFS,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HMBOX1,HMGB2,IGFBP3,MCM2,MCM3,MCM6,MSH2,NCOR2,NEK2,POLD1,RAD51,STAG3,THOC3,TIMELESS,TOP2A,UHRF1
GO:0032993	CC	Protein–DNA complex	10	20	H2BFS,HHEX,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,MCM3,POLD1
GO:0044454	CC	Nuclear chromosome part	10	40	BRD8,BUB1,CCNB1,CDCA5,CHAF1A,CHAF1B,DNMT3B,ENC1,EZH2,H2BFS,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HMBOX1,HMGB2,IGFBP3,MCM2,MCM3,MCM6,MSH2,NCOR2,POLD1,RAD51,STAG3,THOC3,TIMELESS,UHRF1
GO:0000790	CC	Nuclear chromatin	10	25	BRD8,CDCA5,CHAF1A,CHAF1B,DNMT3B,ENC1,EZH2,H2BFS,HIST1H1C,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HMGB2,IGFBP3,NCOR2,TIMELESS,UHRF1
GO:0046983	MF	Protein dimerization activity	10	47	AHR,ASNS,BARD1,BIRC5,BTBD11,CD2,CD3D,CENPF,DPP4,E2F8,FAP,GZMA,H2BFS,HHEX,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HLA-DQB1,HOMER1,HPGD,KIT,LCN2,MAD2L1,MAT1A,MSH2,NCOA6,NR0B1,NR3C1,RAB11FIP4,SRGAP2,TCFL5,TIMELESS,TOP2A,TYMS,UGT1A6
GO:0046982	MF	Protein heterodimerization activity	5.938270754	27	AHR,BARD1,BIRC5,BTBD11,CD3D,H2BFS,HIST1H2BB,HIST1H2BC,HIST1H2BD,HIST1H2BE,HIST1H2BF,HIST1H2BH,HIST1H2BI,HIST1H2BJ,HIST1H2BL,HIST1H2BN,HIST1H2BO,HIST1H4F,HIST1H4H,HIST1H4J,HIST1H4K,HLA-DQB1,HOMER1,NR3C1,TIMELESS,TOP2A,UGT1A6
GO:0004556	MF	Alpha-amylase activity	4.35364509	03	AMY1A,AMY2A,AMY2B
GO:0005201	MF	Extracellular matrix structural constituent	4.343857181	08	COL14A1,COL1A1,COL27A1,COL3A1,COL4A5,COL5A2,LAMB1,MATN3
GO:0000217	MF	DNA secondary structure binding	4.305114444	05	HMGB2,HMGB3,MSH2,NR0B1,RAD51

Table 5 (continued)

GO ID	CATEGORY	GO name	LogP	Gene count	Genes
GO:0043142	MF	Single-stranded DNA-dependent ATPase activity	4.183384389	04	CHTF18,RAD51,RFC4,RFC5
GO:0000400	MF	Four-way junction DNA binding	3.935156577	04	HMGB2,HMGB3,MSH2,RAD51
GO:0042802	MF	Identical protein binding	3.827105432	41	ANXA4,ASNS,BARD1,BIRC5,CD2,CENPF,CHAF1A,CLDN1,COL1A1,DPP4,E2F8,FAP,FHOD1,FN1,GZMA,HHEX,HOMER1,HPGD,HSPB1,IER5,KIT,LCN2,MAD2L1,MAT1A,MCM6,MMP9,MSH2,NCOA6,NR0B1,NR3C1,PPP1R13L,PRC1,RAB11FIP4,RAD51,SRGAP2,TIMELESS,TK1,TOP2A,TYMS,UGT1A6,UHRF1
GO:0008301	MF	DNA binding, bending	3.532716498	04	HHEX,HMGB2,HMGB3,TOP2A
GO:0033170	MF	Protein–DNA loading ATPase activity	3.45087681	03	CHTF18,RFC4,RFC5

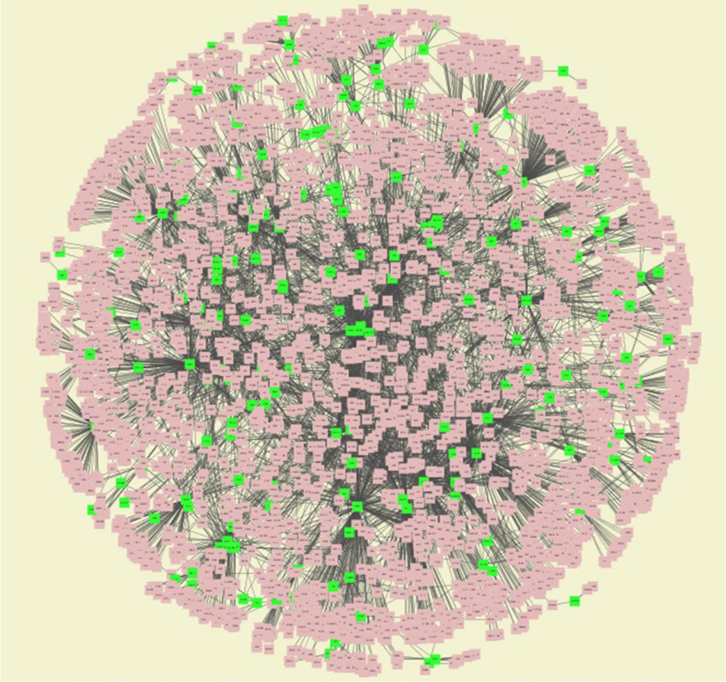


Fig. 5 Protein–protein interaction (PPI) networks for differentially-expressed genes (DEGs). (Green round shape node represents upregulated genes). Green dots are also genes which are not hub or differential expressed genes

(degree = 100). Module 8 had 36 nodes and 74 edges. Hub genes in this modules such as UBD (degree = 664), MAGED2 (degree = 37), HIST1H1C (degree = 144), MAD2L1 (degree = 60), and PHGDH (degree = 76). Module 10 had 29 nodes and 89 edges. Hub genes in this modules such as HSPB1 (degree = 129), HIST1H2BJ (degree = 23), VCAM1 (degree = 671), UHRF1 (degree = 35), MCM3 (degree = 126), NCOR2 (degree = 140), HIST1H1C (degree = 144), TOP2A (degree = 110), FN1 (degree = 1012), PBK (degree = 91), ASNS (degree = 43), MCM2 (degree = 110), TMPO (degree = 58), MCM6 (degree = 100), HMGB2 (degree = 39), HIST1H2BL (degree = 21), TYMS (degree = 39), CHAF1B (degree = 26), and PHGDH (degree = 76). Module 27 had 17 nodes and 47 edges. Hub genes in this modules such as CCNE1 (degree = 84), POLD1 (degree = 67), CDT1 (degree = 55), and PRC1 (degree = 27).

Construction of target genes–miRNA regulatory network

Target genes (up and down regulated) interacts with miRNA are shown Figs. 12 and 13. Top five up regulated targeted genes such as YWHAZ interacts with 212 miRNAs, GATA6 interacts with 207 miRNAs, LDLR interacts with 167 miRNAs, BZW1 interacts with 149 miRNAs, and IGFBP5

Table 6 Topology table for up and down regulated genes

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Up	YWHAZ	805	0.260189	1.11E+08	0.402117	0.001715
Up	HSPA5	394	0.102115	43035116	0.382252	0.004056
Up	STAT3	213	0.051796	22678172	0.352206	0.006511
Up	APOE	183	0.031537	14772964	0.336713	0.029905
Up	GRK5	175	0.038557	10896884	0.353572	0.006043
Up	STAT1	174	0.037604	18747672	0.34399	0.005182
Up	ICAM1	169	0.030647	27529814	0.322755	0
Up	HP	160	0.014866	10983432	0.317342	0.038836
Up	APOC1	151	0.011857	5833358	0.305657	0.044531
Up	SH3BP5	142	0.014981	9089406	0.332427	0.049146
Up	TH	142	0.051469	12072240	0.329652	9.25E−04
Up	SERPING1	137	0.009915	5551286	0.311991	0.053456
Up	NR4A1	116	0.028826	6514160	0.361448	0.008096
Up	MAP3K5	113	0.022897	8301864	0.355024	0.011852
Up	CD83	111	0.04396	5160850	0.323067	0
Up	SF1	103	0.018338	11066854	0.323005	3.81E−04
Up	PRKAR1A	102	0.021773	8972204	0.330455	0.002136
Up	NOLC1	99	0.013941	4681102	0.353123	0.021439
Up	IRS1	99	0.020333	5412970	0.357199	0.010513
Up	HOXB2	90	0.028436	23027092	0.255816	0
Up	NDRG1	89	0.011654	4885178	0.333134	0.00715
Up	UCHL1	84	0.014764	5396790	0.351367	0.016064
Up	CEBPB	83	0.013172	6893876	0.33516	0.013811
Up	CDH2	77	0.020705	4804698	0.324867	0.002051
Up	CXCL2	75	0.024541	15362666	0.270457	0
Up	PCK1	72	0.011033	6295012	0.32386	0
Up	THBS1	72	0.023065	6023294	0.328077	0.004695
Up	FUBP1	70	0.014474	6469484	0.323672	0
Up	S100A8	61	0.012758	4874700	0.325268	0.009836
Up	GPRASP1	54	0.014613	2698352	0.318896	6.99E−04
Up	JUNB	54	0.011046	4382718	0.319302	0.003771
Up	CASP9	53	0.010001	3394028	0.317261	0
Up	IPO7	47	0.006543	1786614	0.340833	0.018501
Up	DLG2	46	0.012177	2037980	0.266844	0.006763
Up	ID2	46	0.009911	1596352	0.333666	0.007729
Up	CHGB	43	0.009814	1350512	0.294042	0.002215
Up	HES1	43	0.009332	2141374	0.339357	0.022148
Up	NEDD9	42	0.007011	1987930	0.317241	0.004646
Up	CCL2	41	0.011504	7709112	0.258507	0
Up	FBLN1	41	0.009905	2238454	0.298968	0.003659
Up	HSPA4L	40	0.005487	1782684	0.323171	0.008974
Up	CYP11A1	38	0.005559	1064806	0.299504	0.048364
Up	IL8	38	0.010663	1850970	0.290162	0
Up	CTSD	37	0.007161	2798138	0.320056	0
Up	PDGFRA	37	0.006507	1365652	0.328593	0.024024
Up	PLAT	34	0.005815	3653930	0.286482	0.008065
Up	MAT2A	34	0.006677	2089346	0.321616	0.005348
Up	SNAI1	34	0.005517	1700822	0.317081	0.005348
Up	IFI27	33	0.01096	1773150	0.317302	0
Up	NEFH	32	0.001249	748058	0.31654	0
Up	VASN	31	0.003535	1424710	0.313062	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Up	DCN	30	0.006619	1598304	0.296108	0.013793
Up	NR4A2	30	0.004686	949674	0.301087	0.009195
Up	ATP5L	30	0.00883	1869502	0.31416	0
Up	STMN2	29	0.006803	1305076	0.318066	0.002463
Up	CALD1	29	0.004111	1314068	0.32203	0.009852
Up	GJA1	29	0.004867	1221800	0.316441	0
Up	AKR1B1	28	0.006739	1201148	0.312555	0
Up	EGR1	28	0.003319	901046	0.299218	0.02381
Up	NR2F1	28	0.005539	1348816	0.321451	0.005291
Up	CEBPD	28	0.003471	1740498	0.321493	0.031746
Up	PC	27	0.002581	734660	0.31654	0.013333
Up	GTPBP4	26	0.001933	1254946	0.320773	0
Up	PEG10	26	0.005379	1219672	0.312535	0
Up	HBB	26	0.004537	943000	0.324132	0.027692
Up	TAGLN	25	0.004812	837454	0.324048	0.023333
Up	PLA2G4A	24	0.003171	1086562	0.31672	0
Up	RALYL	23	0.004771	1004328	0.312438	0
Up	ERN1	22	0.004599	812102	0.331526	0.047619
Up	PHF10	22	0.003526	1193074	0.31416	0
Up	LDLR	22	0.004787	788738	0.333955	0.030303
Up	GNAZ	21	0.004054	898038	0.314594	0
Up	PRKAR2B	20	0.002942	708156	0.315445	0.005263
Up	NPY	20	0.005686	2111722	0.232668	0
Up	NPTX1	20	0.004764	800220	0.313003	0
Up	FRMD5	20	0.003025	825016	0.318673	0.010526
Up	CPE	20	0.003275	694146	0.312282	0
Up	BZW1	19	0.003467	835164	0.312263	0
Up	DNAJB9	18	0.002916	442302	0.327605	0.026144
Up	MAPK4	18	0.003071	706658	0.312301	0
Up	GEM	17	0.004142	2647996	0.255178	0
Up	NOV	17	0.002335	381924	0.286547	0.029412
Up	GCLM	17	0.00366	727990	0.312185	0
Up	ABCB1	16	0.002381	588236	0.314831	0
Up	DLL1	16	0.004228	463166	0.312847	0.010989
Up	ALAS1	16	0.002042	544864	0.313434	0
Up	ELL2	16	0.003098	550500	0.311719	0
Up	CNN1	16	0.002686	559686	0.311661	0
Up	FZD4	16	0.0062	1151652	0.316321	0.016667
Up	HAND2	15	0.002619	900578	0.320445	0
Up	CYP4B1	15	0.005577	2153326	0.224119	0
Up	TFAP2B	15	0.0051	647930	0.31686	0
Up	STARD13	15	0.002381	353350	0.28604	0.009524
Up	SAA1	15	0.005577	2536086	0.208413	0
Up	ALDH3A2	15	0.002173	632486	0.312204	0
Up	PTGIR	15	0.002903	590314	0.312477	0
Up	NBEA	15	0.002438	483344	0.312418	0.009524
Up	PRKD3	15	0.00209	519966	0.311777	0
Up	SERP1	15	0.002939	2565110	0.268157	0
Up	MRAS	15	0.002402	387842	0.311913	0
Up	HOXA5	14	0.00233	577318	0.313375	0
Up	TGFBR3	14	0.003178	2040990	0.257816	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Up	CXCL12	14	0.002273	1405652	0.263105	0
Up	CYP11B2	14	0.004781	816660	0.231103	0.010989
Up	IER3	14	0.002368	726758	0.318147	0
Up	NPC1	13	0.003237	392086	0.311216	0
Up	LITAF	13	0.001483	416406	0.313669	0
Up	LXN	13	0.003209	2483028	0.241313	0
Up	NFIL3	13	0.00244	611732	0.315644	0
Up	NAP1L5	13	0.002263	590066	0.312828	0
Up	SCARB1	13	8.76E−04	240620	0.318592	0.054545
Up	SNAPC1	13	0.003388	275926	0.323067	0.025641
Up	FGF7	13	0.001482	827852	0.243493	0
Up	MCF2	13	0.003037	781350	0.31271	0
Up	MSI2	13	2.53E−04	169164	0.312204	0
Up	NGEF	13	0.002503	1463194	0.243836	0
Up	MTSS1	13	0.001506	297038	0.311409	0
Up	PTP4A1	13	0.002681	518420	0.314338	0
Up	EDNRB	12	0.002133	535188	0.314574	0
Up	SCAP	12	0.001705	292106	0.311448	0
Up	C1S	12	0.001068	358418	0.269078	0.111111
Up	PAPSS2	12	0.001417	382838	0.313512	0
Up	QPCT	11	2.63E−04	274286	0.314318	0
Up	CITED1	11	9.91E−04	295604	0.283533	0
Up	SDF2L1	11	0.001197	324840	0.315128	0
Up	SYT4	11	0.002102	163066	0.251833	0
Up	IGFBP2	11	0.001246	299658	0.232334	0.090909
Up	CD38	11	0.002815	1432210	0.242351	0
Up	ZNF331	11	0.001416	301766	0.31686	0.018182
Up	KCNK3	10	0.001207	396662	0.293199	0.133333
Up	DHCR24	10	0.002198	505154	0.314851	0
Up	FDX1	10	0.001274	243338	0.254789	0.071429
Up	CCL13	10	0.001727	1328302	0.252977	0
Up	RAB38	10	3.56E−04	224944	0.314023	0
Up	SLC25A19	10	0.003217	342904	0.311139	0
Up	DNAJC3	10	6.45E−04	246138	0.312049	0
Up	CXCL1	9	0.002025	923204	0.20422	0
Up	LUM	9	0.00125	818192	0.233927	0
Up	FGF23	9	0.002395	982630	0.235853	0
Up	CNN3	9	0.001959	435914	0.314693	0.055556
Up	TBX3	9	2.22E−04	139790	0.268804	0
Up	CYP17A1	9	0.002402	1038928	0.246352	0
Up	MRAP	9	3.66E−04	28306	0.239252	0.285714
Up	TLX2	9	0.001653	707066	0.242679	0
Up	P2RY2	9	4.77E−04	216178	0.314101	0
Up	RAB34	9	9.30E−04	216324	0.313101	0
Up	ABR	9	8.46E−04	339040	0.31361	0
Up	GRIK1	9	0.001453	219726	0.312263	0
Up	INSM1	9	0.001412	1179748	0.249205	0
Up	FOXK2	9	0.001343	957336	0.258667	0
Up	ARFGAP3	8	0.003507	406866	0.318977	0
Up	PTX3	8	4.37E−04	135044	0.225399	0.107143
Up	IL1RL1	8	0.001622	1169410	0.257789	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Up	SCG2	8	0.001484	472656	0.315644	0
Up	ATP1B3	8	5.56E−04	251508	0.311719	0
Up	SLC27A6	8	9.25E−04	223448	0.31236	0
Up	RPRM	8	9.73E−04	602230	0.265713	0
Up	ANGPTL4	8	1.16E−04	94094	0.269875	0
Up	ADM	8	6.45E−04	312648	0.221095	0
Up	DUSP16	8	2.75E−04	199746	0.257564	0
Up	IL6	8	0.001595	1278764	0.211991	0
Up	FOSL2	8	6.37E−04	426608	0.318916	0.107143
Up	FGF12	8	3.20E−04	260234	0.261882	0
Up	ALDH1A1	8	0.001334	246562	0.311855	0
Up	CTH	8	0.001259	181134	0.337189	0.035714
Up	HSPA1A	7	3.86E−04	465632	0.310792	0.190476
Up	SEMA6A	7	0.001436	568036	0.256589	0
Up	CLDN5	7	9.05E−04	116514	0.311255	0
Up	ADAMTS1	7	0.001315	328126	0.313944	0
Up	CGNL1	7	8.22E−05	67972	0.336352	0.285714
Up	MT1A	7	0.001392	337106	0.311409	0
Up	ADH1B	7	0.001596	934364	0.245736	0
Up	ACVR1C	7	9.66E−04	421426	0.248206	0
Up	CHGA	7	0.001402	325618	0.314732	0
Up	NR4A3	6	8.11E−04	622340	0.260942	0
Up	SOAT1	6	9.01E−04	139774	0.311293	0
Up	NRXN3	6	4.91E−04	75632	0.244968	0
Up	FXC1	6	4.24E−04	239412	0.214659	0
Up	CDH18	6	0.001712	212558	0.311158	0
Up	SLC1A2	6	6.26E−06	6146	0.256457	0
Up	DBH	6	0.001595	288082	0.193084	0
Up	TMOD1	6	8.63E−04	664496	0.2457	0
Up	ABTB2	6	3.90E−04	251672	0.314377	0
Up	UNC5B	6	0.001994	195650	0.310984	0
Up	CRH	6	1	12	1	0
Up	SEMA3B	6	0.001196	833496	0.176276	0
Up	PGM3	6	8.64E−04	224062	0.313336	0
Up	MAP6	6	4.20E−04	39634	0.270034	0
Up	MGST1	6	5.54E−04	92244	0.310907	0
Up	GIPC2	5	4.09E−04	258822	0.20672	0
Up	CD163	5	2.02E−04	49098	0.282638	0
Up	MFAP4	5	8.65E−04	362414	0.2551	0
Up	TNXB	5	4.17E−04	170710	0.224752	0
Up	PID1	5	0.001595	716732	0.204478	0
Up	AOX1	5	5.59E−04	43716	0.256891	0
Up	CRLF1	5	1	20	1	0
Up	IL1R2	5	0.001595	463204	0.206814	0
Up	WFDC1	5	0.001208	462728	0.230148	0
Up	ADRA2C	5	0.001196	466068	0.288941	0.1
Up	FMOD	5	1.55E−05	8296	0.204403	0
Up	SLC2A3	5	9.84E−04	265230	0.312496	0
Up	AASS	5	2.52E−04	144854	0.314456	0
Up	AOC3	4	0.001196	202014	0.243789	0
Up	DDC	4	4.35E−04	367046	0.23763	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Up	TIPARP	4	4.32E−04	70204	0.31201	0
Up	FCN2	4	4.02E−04	240944	0.205736	0
Up	FGF9	4	7.65E−06	7000	0.237675	0
Up	PDK4	4	6.23E−04	90866	0.310907	0
Up	DUSP5	4	5.68E−05	101818	0.31491	0
Up	ADH1A	4	2.29E−06	1694	0.229358	0
Up	PON1	4	1.36E−05	12094	0.24041	0
Up	GPM6B	4	4.72E−04	222612	0.269671	0
Up	ANGPTL1	4	3.99E−04	416572	0.147168	0
Up	NPY1R	4	8.50E−04	120958	0.210372	0
Up	SRPX2	4	7.98E−04	475448	0.202889	0
Up	DNER	4	8.00E−04	368526	0.210965	0
Up	GCKR	4	4.32E−04	59448	0.311487	0
Up	PLEK2	4	7.91E−05	22100	0.310907	0
Up	PSD3	4	8.50E−04	91062	0.310907	0
Up	KCNK5	3	4.30E−04	112320	0.312769	0
Up	RAB20	3	0	0	0.310792	0
Up	DNAJC12	3	6.42E−05	13030	0.254092	0
Up	TPMT	3	4.08E−05	78824	0.312945	0
Up	CHRNA3	3	7.98E−04	165798	0.205787	0
Up	PDE8A	3	2.85E−05	38286	0.311409	0
Up	MT1G	3	2.41E−04	69528	0.310869	0
Up	ENPP2	3	2.00E−05	16510	0.244347	0
Up	TMEM25	3	7.98E−04	518454	0.230084	0
Up	ST3GAL4	3	7.98E−04	78266	0.310869	0
Up	C7	3	4.06E−04	114772	0.218446	0
Up	RGN	2	3.99E−04	160892	0.203755	0
Up	ARHGAP18	2	1	2	1	0
Up	TNRC4	2	3.99E−04	150222	0.224029	0
Up	AQP11	2	2.26E−06	2146	0.245881	0
Up	PENK	2	1.45E−04	30688	0.31083	0
Up	FJX1	2	1	2	1	0
Up	TIMP4	2	2.09E−05	25638	0.199245	0
Up	AGXT2L1	2	3.15E−05	65752	0.31273	0
Up	SLC33A1	2	8.92E−06	7402	0.310869	0
Up	CYP26B1	2	4.25E−06	3524	0.259551	0
Up	FMO3	2	1	2	1	0
Up	MT1F	2	4.50E−05	29954	0.31083	0
Up	PNMT	2	1.66E−06	476	0.217141	0
Up	ADH1C	2	0	0	0	0
Up	MARCO	2	1	2	1	0
Up	ALDH1A3	2	1.95E−05	39422	0.311932	0
Up	GSTA4	2	1.93E−05	16030	0.311235	0
Up	SELK	1	0	0	0.201892	0
Up	ADAMTS9	1	0	0	0.202709	0
Up	DKK3	1	0	0	0.217962	0
Up	BHMT2	1	0	0	0.244944	0
Up	ARHGAP36	1	0	0	0.139309	0
Up	TCEAL7	1	0	0	0.22427	0
Up	NRXN3	1	0	0	0.231668	0
Up	AS3MT	1	0	0	0.310792	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Up	HEPH	1	0	0	0.236621	0
Up	SLC16A9	1	0	0	0.310792	0
Up	AK7	1	0	0	0.310792	0
Up	PHOX2B	1	0	0	0.310792	0
Up	MEDAG	1	0	0	0.232097	0
Up	HSD3B2	1	0	0	0.243717	0
Up	G0S2	1	0	0	0.196174	0
Up	MT1E	1	0	0	0.310792	0
Up	FNDC4	1	0	0	0.209949	0
Down	FN1	1012	0.247108	3.59E+08	0.420735	0.001521
Down	VCAM1	671	0.114671	2.23E+08	0.392524	0.001188
Down	UBD	664	0.148922	2.86E+08	0.375756	6.22E−04
Down	BARD1	252	0.051185	43410948	0.34989	0.001644
Down	TK1	169	0.044886	10192580	0.378831	0.003593
Down	HIST1H1C	144	0.015213	9591504	0.360158	0.018648
Down	CDH1	142	0.027298	21140776	0.341423	0.004295
Down	NCOR2	140	0.02482	11862242	0.351193	0.012436
Down	BBC3	137	0.003747	3868982	0.338248	0.040907
Down	CABLES1	135	0.003566	3907198	0.341445	0.041238
Down	HSPB1	129	0.025742	8109468	0.374183	0.006662
Down	MCM3	126	0.018368	7052976	0.390927	0.034667
Down	CCNB1	114	0.011201	5506412	0.350131	0.020183
Down	TOP2A	110	0.010841	5482028	0.377511	0.030692
Down	MCM2	110	0.013514	5285790	0.375562	0.032193
Down	KIT	101	0.025615	9413426	0.33136	0
Down	MCM6	100	0.012057	4474220	0.380614	0.044242
Down	RAD51	92	0.016949	7408576	0.339873	0.008839
Down	PBK	91	0.008987	7594990	0.348406	0.006105
Down	OGT	88	0.019919	8032948	0.330243	0
Down	CHAF1A	86	0.007639	6935084	0.327629	0.012312
Down	CCNE1	84	0.0092	4149564	0.347289	0.02008
Down	COL1A1	84	0.022799	3131070	0.36488	0.011761
Down	FANCA	78	0.010603	6286322	0.341491	0.01665
Down	PHGDH	76	0.011527	4602752	0.381384	0.015789
Down	DDB2	71	0.008592	4100072	0.335264	0.013682
Down	DNMT3B	67	0.007798	3188916	0.337934	0.019901
Down	POLD1	67	0.008216	3852240	0.341491	0.019448
Down	PSAT1	63	0.007014	3683060	0.34571	0.012801
Down	SLPI	60	0.021133	46566718	0.255904	0
Down	MAD2L1	60	0.010914	2524392	0.350492	0.014124
Down	TMPO	58	0.006787	2517242	0.348931	0.006655
Down	CDT1	55	0.003614	1890066	0.343889	0.052975
Down	CHTF18	53	0.005028	3377516	0.331965	0.019594
Down	RFC5	49	0.00227	1556158	0.330671	0.033163
Down	HIST1H2BB	49	0.003786	1987842	0.3308	0.002551
Down	XRCC1	49	0.006593	3001388	0.332246	0.011905
Down	DYRK2	46	0.004914	3770024	0.32958	0
Down	ZWINT	45	0.006455	2262864	0.333159	0.055556
Down	MYBL2	44	0.004415	1611182	0.319892	0.014799
Down	BUB1	44	0.00463	1759430	0.337441	0.059197
Down	NUP107	43	0.006203	2033446	0.344797	0.015504

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Down	AHR	43	0.005211	2084556	0.332333	0.013289
Down	ASNS	43	0.006628	1689542	0.344704	0.011074
Down	NEK2	42	0.006389	1600920	0.332832	0.011614
Down	TPX2	41	0.0051	2502284	0.330114	0.005398
Down	FANCG	40	0.004436	1407882	0.335419	0.037179
Down	GUSB	40	0.00753	2561542	0.326768	0
Down	BIRC5	40	0.00544	1811080	0.336616	0.019231
Down	HMGB2	39	0.005917	1912668	0.369138	0.047233
Down	ULK1	39	0.007587	2196048	0.327187	0
Down	IQGAP2	39	0.005949	2315186	0.329601	0
Down	TYMS	39	0.008842	1290842	0.344564	0.006006
Down	MAGED2	37	0.004855	1598934	0.344168	0.015015
Down	LGALS3	36	0.005086	1308158	0.315454	0.001587
Down	NOTCH2	36	0.006795	1629564	0.327419	0.004762
Down	IGFBP3	35	0.00667	1560520	0.334516	0.026891
Down	GMNN	35	0.006171	1415874	0.335463	0.026891
Down	UHRF1	35	0.002532	1021952	0.344098	0.097479
Down	SMYD2	35	0.005435	1625366	0.305868	0.001681
Down	PTTG1	34	0.002712	1090242	0.338001	0.024955
Down	RALGDS	32	0.005278	3046896	0.290564	0
Down	MAPKAPK5	31	0.005277	1074812	0.331015	0.010753
Down	PDCD4	30	0.00258	1535918	0.329452	0
Down	SMS	30	0.005878	1331616	0.334208	0.009195
Down	PPP1R13B	30	0.004852	1495046	0.328411	0.011494
Down	LAMB1	30	0.005385	1312774	0.326642	0
Down	FHOD1	29	0.005336	1673834	0.330007	0.007389
Down	PRC1	27	0.002866	992622	0.338856	0.07
Down	HOMER1	27	0.006992	979294	0.325265	0.006667
Down	TTK	26	0.003871	953520	0.333945	0.012308
Down	CHAF1B	26	8.92E−04	550478	0.343796	0.123077
Down	RAI14	25	0.003301	862300	0.334472	0.01
Down	KIAA0101	25	0.004294	912054	0.328708	0.006667
Down	CDCA8	24	0.00349	912220	0.330093	0.036232
Down	SPAG5	24	0.005556	663242	0.333355	0.007246
Down	CCNB2	24	0.004868	588930	0.336394	0.039855
Down	TIMELESS	24	0.004962	1034812	0.328305	0.014493
Down	KIF11	24	0.00262	663088	0.342525	0.025362
Down	DPP4	24	0.005942	525344	0.272849	0.004329
Down	HMMR	23	0.001472	657140	0.329069	0.01581
Down	EXO1	23	8.12E−04	567130	0.330865	0.059289
Down	HIST1H2BJ	23	0.004115	638996	0.358864	0.023715
Down	TGFA	22	0.004551	2638492	0.280854	0
Down	HIST1H2BL	21	0.001445	722188	0.35598	0.02381
Down	SPARC	21	0.001615	297382	0.319671	0.095238
Down	RABEP2	20	0.002531	489734	0.332832	0.036842
Down	PTPN3	19	0.001936	1281432	0.291578	0
Down	MYO10	19	0.001708	524684	0.334406	0.023392
Down	CDCA5	19	0.003513	562400	0.333683	0.005848
Down	CD3D	19	0.003005	557940	0.332898	0.017544
Down	ULK2	19	0.001922	1184198	0.288997	0
Down	PMAIP1	18	0.002005	734266	0.328729	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Down	RRM2	18	0.001888	628902	0.352457	0.084967
Down	GRB14	18	0.002233	955212	0.287059	0
Down	FBXO32	18	0.002695	615316	0.324809	0
Down	HMGB3	18	0.002091	510236	0.324643	0
Down	NR0B1	17	0.00153	285264	0.332572	0.029412
Down	CLDN1	17	0.002751	968092	0.274378	0
Down	PHF17	17	0.001222	366348	0.331554	0.007353
Down	ANXA4	17	0.002387	514786	0.334362	0.022059
Down	JAG1	16	0.0023	419260	0.327272	0.025
Down	FGG	16	0.002573	1752368	0.305409	0.041667
Down	DDX3Y	16	0.001334	343024	0.341148	0.008333
Down	HIST1H2BO	15	9.90E−04	269742	0.325286	0
Down	MELK	15	0.002253	511338	0.325348	0
Down	LIG1	15	0.001271	409294	0.325785	0
Down	ASPM	15	0.001185	377710	0.327272	0.009524
Down	COL3A1	15	5.63E−04	97696	0.289671	0.028571
Down	PLK2	15	0.002236	543740	0.327651	0
Down	RAD51AP1	14	0.002545	393046	0.281102	0.030303
Down	TXNIP	14	0.002282	1018820	0.328517	0
Down	ADA	14	0.005195	484338	0.33388	0.030303
Down	NUDT1	14	0.001469	394702	0.325411	0
Down	HHEX	14	0.003206	474668	0.324829	0
Down	STK36	13	0.002692	447454	0.325224	0
Down	HIST1H2BD	13	1.57E−04	144842	0.325515	0
Down	BMF	13	0.001709	727030	0.245777	0
Down	HMBOX1	13	0.002014	1268808	0.296019	0
Down	RHOBTB3	13	0.002321	265950	0.330157	0.076923
Down	ENC1	12	6.21E−04	256316	0.32539	0
Down	HIST1H2BN	12	1.97E−04	130718	0.324416	0
Down	ANGPT2	12	0.001576	259768	0.324519	0
Down	GGH	12	0.001043	302968	0.325515	0
Down	ANLN	12	6.12E−04	300828	0.326558	0
Down	CCDC14	12	0.001011	400232	0.327798	0
Down	PLAGL1	12	1.69E−04	154336	0.325244	0
Down	CDKN3	11	9.33E−04	140242	0.333115	0.083333
Down	PPP1R13L	11	1.14E−04	110084	0.333552	0.109091
Down	SEMG1	11	0.001465	655500	0.328665	0
Down	ROR1	11	0.00147	342152	0.328009	0.018182
Down	HLA-DRB4	11	0.001592	1335524	0.28238	0
Down	RAB11FIP4	11	0.001465	267764	0.325515	0.054545
Down	LAMA3	10	0.001221	931380	0.262512	0
Down	KIF22	10	7.41E−04	204410	0.324974	0
Down	CAP2	10	8.59E−04	214118	0.324871	0
Down	HRK	10	8.77E−04	399988	0.271323	0
Down	CCNG2	9	0.001107	277006	0.325723	0
Down	CCL19	9	0.001989	217540	0.324374	0
Down	CSRP2BP	9	0.001973	763238	0.283354	0
Down	KCNK1	9	0.002024	347846	0.325099	0
Down	AMY2A	9	0.002365	1217106	0.228611	0
Down	IQSEC1	9	0.001581	1239020	0.272922	0
Down	FCER1A	9	0.001184	2647644	0.242639	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Down	LGALS2	9	4.38E−04	250216	0.277805	0
Down	HIST1H2BH	9	1.45E−04	96522	0.324333	0
Down	KNTC1	9	0.001621	254328	0.324209	0
Down	GRIN2C	8	0.001273	887086	0.233957	0
Down	MCM8	8	3.94E−06	4304	0.284748	0.214286
Down	WNT5A	8	0.001992	227064	0.326956	0.035714
Down	MYO5C	8	6.32E−04	171700	0.333923	0.071429
Down	SULT2A1	7	8.32E−04	1150184	0.279728	0
Down	ZNF133	7	1.91E−04	131456	0.271323	0
Down	RPS4Y1	7	7.04E−05	84962	0.324519	0
Down	HLA-DQB1	7	0.00164	192842	0.324374	0
Down	ZNF302	7	4.24E−04	330364	0.271366	0
Down	NEK3	7	0.001577	210734	0.269015	0
Down	TMPO	7	7.82E−05	68978	0.279405	0
Down	SMCR7	7	0.001049	138508	0.324292	0
Down	DEPDC7	6	6.14E−05	37274	0.324395	0
Down	IGLL1	6	4.77E−05	17578	0.257991	0.133333
Down	MICB	6	0.001451	216512	0.325016	0
Down	MICA	6	1.62E−04	25658	0.262161	0
Down	IDH2	6	9.97E−04	191204	0.32456	0
Down	RANBP17	6	0.001963	198960	0.323941	0
Down	RHOBTB2	6	4.30E−04	106422	0.266301	0.133333
Down	CDCA2	6	1.77E−04	119064	0.334164	0.266667
Down	AMY1A	6	0.001763	858042	0.228878	0
Down	MATN3	6	7.85E−04	1895456	0.231101	0
Down	NPTX2	6	0.001576	633864	0.261434	0
Down	RAD54L	6	7.24E−04	103848	0.327124	0.066667
Down	MUC20	5	7.85E−04	602750	0.203744	0
Down	CKAP2	5	9.24E−05	39134	0.324312	0
Down	APOBEC3B	5	6.39E−04	134450	0.324106	0
Down	CXCL9	5	0.001197	138304	0.218837	0
Down	PLA2G1B	5	0.001183	202384	0.213382	0
Down	LTB	4	8.04E−04	253390	0.224105	0
Down	HSD11B2	4	6.40E−06	4664	0.265136	0
Down	MAT1A	4	7.99E−04	96208	0.323859	0
Down	TBC1D8	4	1.66E−04	80092	0.325327	0
Down	LCN2	4	9.09E−05	24174	0.237635	0
Down	FZD6	4	8.03E−04	137772	0.324892	0
Down	ZG16B	4	4.54E−04	73694	0.324292	0
Down	EML1	4	0.001178	265560	0.220343	0
Down	ZNF266	4	7.34E−04	86728	0.324312	0
Down	SPRR1A	4	7.91E−04	265002	0.2566	0
Down	CYP3A5	4	1	12	1	0
Down	IGJ	3	1.10E−04	38948	0.324788	0.333333
Down	COL5A2	3	9.68E−05	22140	0.324622	0.333333
Down	MLF1IP	3	4.55E−06	1770	0.247245	0.333333
Down	OSBPL6	3	4.50E−05	11194	0.25548	0
Down	POPDC2	3	1	6	1	0
Down	KLK1	3	3.93E−04	494842	0.228693	0
Down	ANKRD23	3	3.98E−04	203384	0.239333	0
Down	GRAMD1C	3	4.31E−04	61178	0.323817	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Down	CDCA7	3	7.97E−05	92342	0.326077	0
Down	DDIT4L	3	3.94E−04	139870	0.209761	0
Down	DONSON	3	3.95E−05	77400	0.325827	0
Down	SULF2	2	6.87E−06	4184	0.324023	0
Down	DSCAM	2	1.27E−05	4762	0.323776	0
Down	PLXDC1	2	6.08E−05	12618	0.323776	0
Down	CD99L2	2	1.88E−05	48768	0.325244	0
Down	PRSS8	2	4.00E−08	2	0.175403	0
Down	FAM54A	2	2.80E−06	3304	0.323817	0
Down	STAG3	2	4.30E−07	464	0.238772	0
Down	FANK1	2	9.60E−07	682	0.237082	0
Down	ZNF443	2	4.29E−05	16418	0.323776	0
Down	PNLIPRP2	2	1	2	1	0
Down	CTSL2	2	3.93E−04	39796	0.323776	0
Down	ZDHHC23	2	3.93E−04	166528	0.245706	0
Down	IER5	2	6.89E−05	4170	0.274393	0
Down	COL27A1	2	1.00E−07	16	0.21879	0
Down	LRIG3	2	3.93E−04	193554	0.256755	0
Down	AMY2B	2	1.13E−06	834	0.237991	0
Down	ESM1	2	3.93E−04	66390	0.198048	0
Down	TPSAB1	2	1.10E−07	68	0.210281	0
Down	TMEM44	1	0	0	0.235362	0
Down	PALMD	1	0	0	0.215249	0
Down	KIAA1407	1	0	0	1	0
Down	GPX8	1	0	0	0.323735	0
Down	CCDC150	1	0	0	0.252204	0
Down	PDE8B	1	0	0	0.323735	0
Down	RAD51	1	0	0	0.253673	0
Down	ST6GALNAC2	1	0	0	0.212005	0
Down	CX3CR1	1	0	0	1	0
Down	APOBEC3A	1	0	0	0.323735	0
Down	PCYOX1L	1	0	0	0.240191	0
Down	EXO1	1	0	0	0.266929	0
Down	RNF44	1	0	0	0.323735	0
Down	XYLT2	1	0	0	0.227651	0
Down	SRCRB4D	1	0	0	0.252204	0
Down	RPS4Y2	1	0	0	0.323735	0
Down	FUK	1	0	0	0.323735	0
Down	Cep192	1	0	0	0.246074	0
Down	ZNF700	1	0	0	0.323735	0
Down	HCP5	1	0	0	0.245683	0
Down	CDH1	1	0	0	0.267349	0
Down	SLC2A4RG	1	0	0	0.243626	0
Down	TIGD7	1	0	0	1	0
Down	HPGD	1	0	0	0.245683	0
Down	TCEA3	1	0	0	1	0
Down	IL20RB	1	0	0	1	0
Down	ZNF618	1	0	0	0.233946	0

Table 6 (continued)

Regulation	Node	Degree	Betweenness	Stress	Closeness	Clustering coefficient
Down	CCDC74A	1	0	0	0.231227	0
Down	PAQR4	1	0	0	0.252204	0
Down	PAQR6	1	0	0	1	0

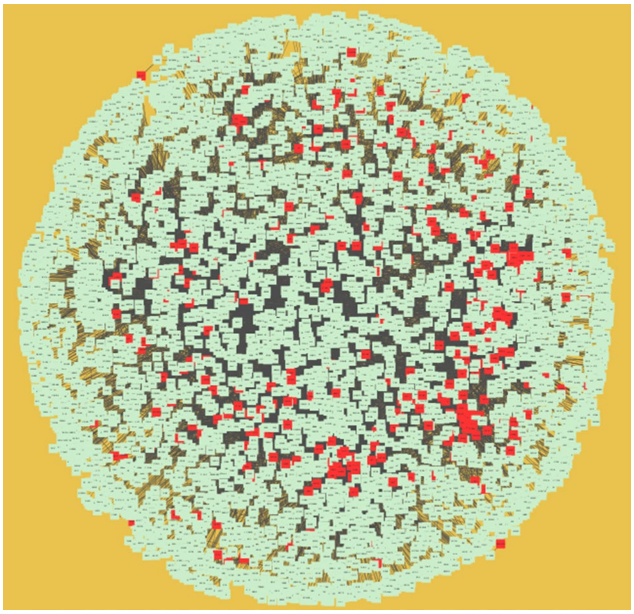


Fig. 6 Protein–protein interaction (PPI) networks for differentially-expressed genes (DEGs). (Pink round shape node represents down-regulated genes). Green dots are also genes which are not hub or differential expressed genes

interacts with 144 miRNAs. Meanwhile, top five down regulated targeted genes such as TXNIP interacts with 228 miRNAs, MAPKAPK5 interacts with 179 miRNAs, PMAIP1 interacts with 147 miRNAs, RAD51 interacts with 147 miRNAs, and MICA interacts with 142 miRNAs (Table 7).

Construction of target genes–TF regulatory network

Target genes (up and down regulated) interacts with TF are shown Figs. 14 and 15. Top five up regulated targeted genes such as HSPA1A interacts with 67 TFs, PHOX2B interacts with 54 TFs, H19 interacts with 52 TFs, CEBPD interacts with 51 TFs, and DNAJC3 interacts with 50 TFs. Meanwhile, top five down regulated targeted genes such as F11R interacts with 91 TFs, CHAF1B interacts with 85 TFs, FANCG interacts with 82 TFs, CENPF interacts with 82 TFs, and XRCC1 interacts with 82 TFs (Table 8).

Survival analysis and stage-related expression analysis of hub genes

TCGA data of ACC patients are used via the UALCAN data portal. Kaplan–Meier curve for overall survival of TCGA patients with ACC is obtained according to the low and high expression of each gene. The results showed that patients in the high mRNA expression group for YWHAZ had worse overall survival than those in the low expression group ($P=0.012$) (Fig. 16a), the high mRNA expression group for STAT1 had worse overall survival than those in the low expression group ($P=0.024$) (Fig. 16b), the high mRNA expression group for ICAM1 had worse overall survival than those in the low expression group ($P=0.008$) (Fig. 16c, a), the high mRNA expression group for SH3BP5 had worse overall survival than those in the low expression group ($P=0.016$) (Fig. 16d), the high mRNA expression group for CD83 had worse overall survival than those in

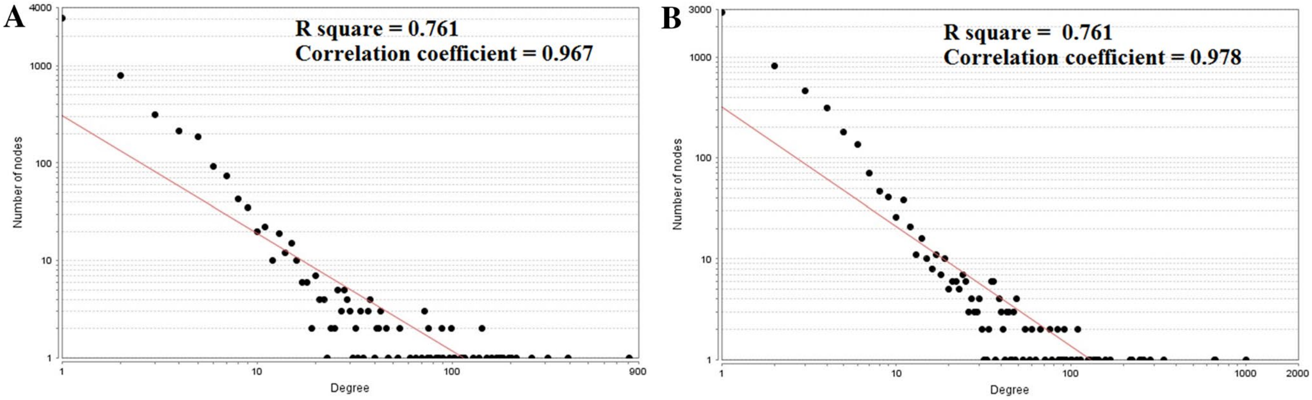


Fig. 7 Node degree distribution for up and down regulated genes. Red lines: regression lines

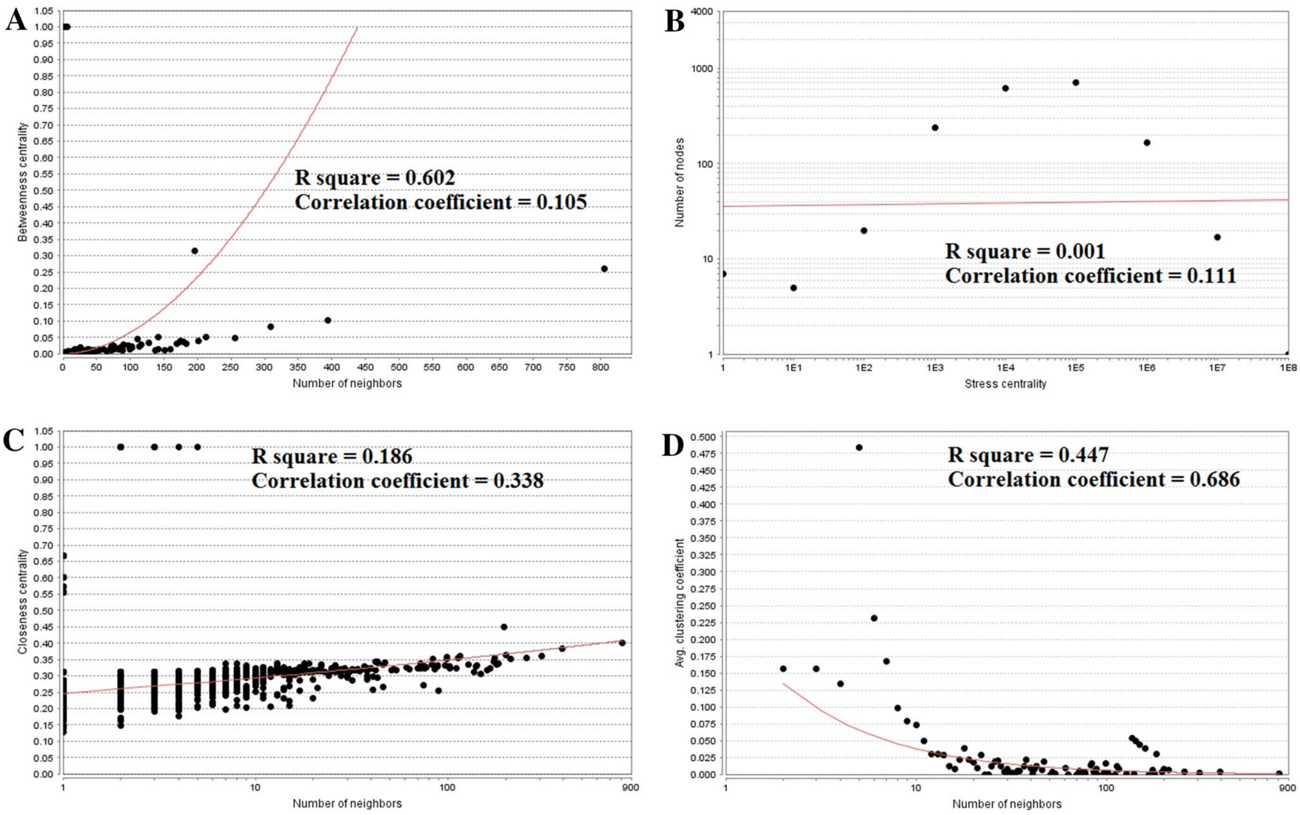


Fig. 8 Regression diagrams for upregulated genes (**a** betweenness centrality; **b** stress centrality; **c** closeness centrality; **d** clustering coefficient). The red straight lines and the red curve lines: regression lines

the low expression group ($P = 0.00016$) (Fig. 16e), the high mRNA expression group for FN1 had worse overall survival than those in the low expression group ($P = 0.0069$) (Fig. 16f), the high mRNA expression group for TK1 had worse overall survival than those in the low expression group ($P = 0.0001$) (Fig. 16g), the high mRNA expression group for HIST1H1C had worse overall survival than those in the low expression group ($P = 0.0057$) (Fig. 16h), the high mRNA expression group for CABLES1 had worse overall survival than those in the low expression group ($P = 0.017$) (Fig. 16i), and the high mRNA expression group for MCM3 had worse overall survival than those in the low expression group ($P = 0.00011$) (Fig. 16j). TCGA data analysis showed that hub genes such as YWHAZ, STAT1, ICAM1, CD83, FN1, TK1, HIST1H1C, and MCM3 were highly expressed in stages 4 (Fig. 17), while hub genes such as SH3BP5 and CABLES1 were highly expressed in stages 2 and stages 1 (Fig. 18).

Genetical alteration of the five hub genes

Five hub genes' alteration statuses in TCGA bladder cancer patients were analyzed using the CbioPortal database. The five hub genes such as YWHAZ, STAT1, SH3BP5, TK1, and HIST1H1C altered in 0% patients, while five hub genes such as ICAM1, CD83, FN1, CABLES1, and MCM3 altered in 3% (missence mutation and amplification) and 1.1% (missence mutation and amplification) patients and the frequency of alteration of each hub gene are shown in Fig. 19.

Discussion

In recent years, although the morbidity of ACC has less, it is still malignant tumors worldwide. Specific biomarkers and effective targets are still needed to be diagnosed.

In this study, a total of 884 DEGs were picked out from the profile of GSE19775, including 441 up regulated genes and 443 down regulated genes. Gene such as phenylethanolamine *N*-methyltransferase (PNMT) [59] and cocaine- and amphetamine-regulated transcript (CART) [60] were associated with development of adrenal pheochromocytoma, but these genes may be responsible for progression of ACC. Methylation inactivation of tumor suppressor gene proenkephalin (PENK) was responsible for development of colorectal cancer [61], but inactivation of this gene may be identified with growth of ACC. Chromogranin A (parathyroid secretory protein 1) (CHGA) was important for progression

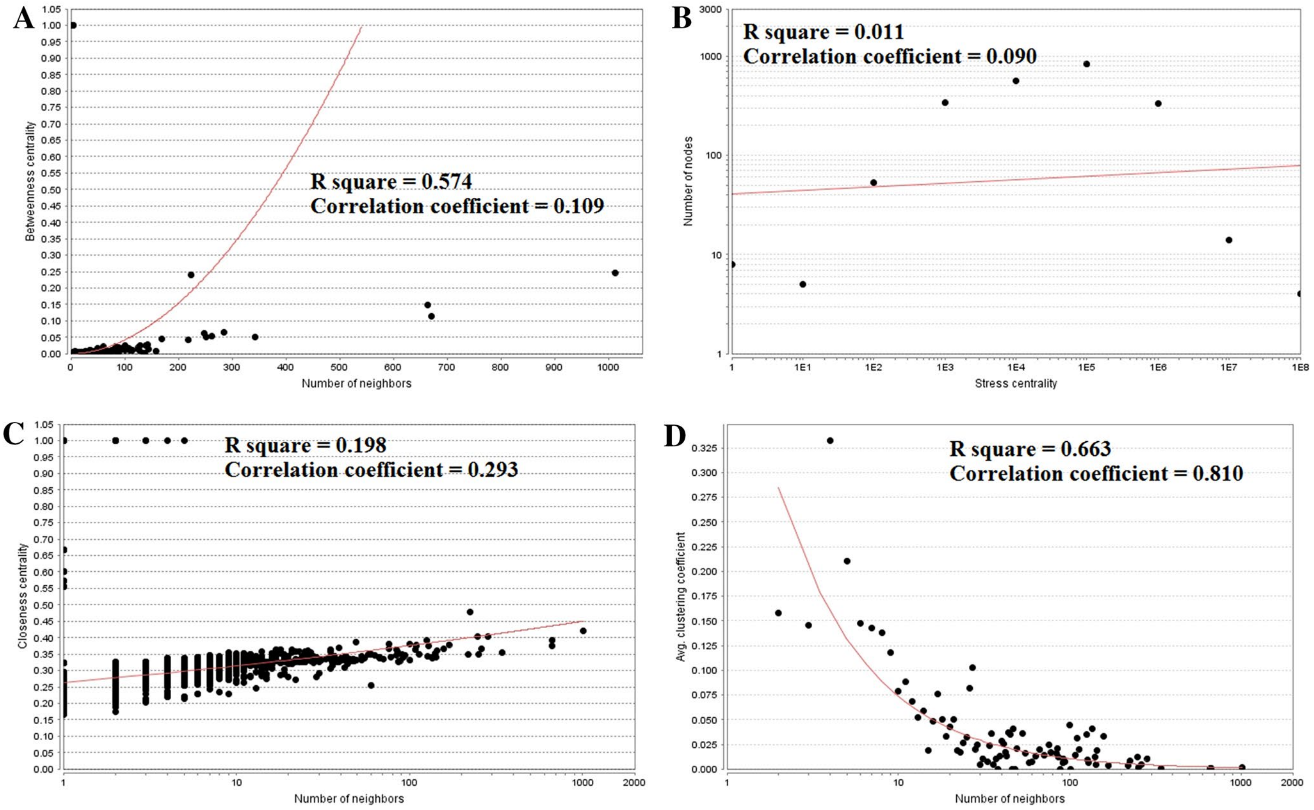
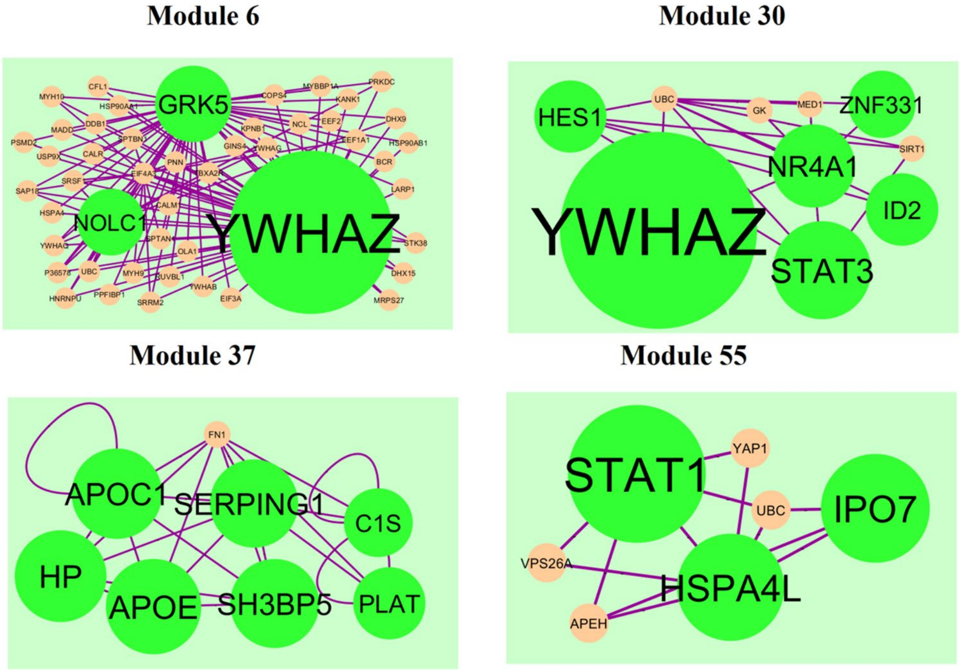


Fig. 9 Regression diagrams for down-regulated genes (**a** betweenness centrality; **b** stress centrality; **c** closeness centrality; **d** clustering coefficient). The red straight lines and the red curve lines: regression lines

Fig. 10 Modules in PPI network. The pink round nodes denote down-regulated genes. Green dots are also genes which are not hub or differential expressed genes



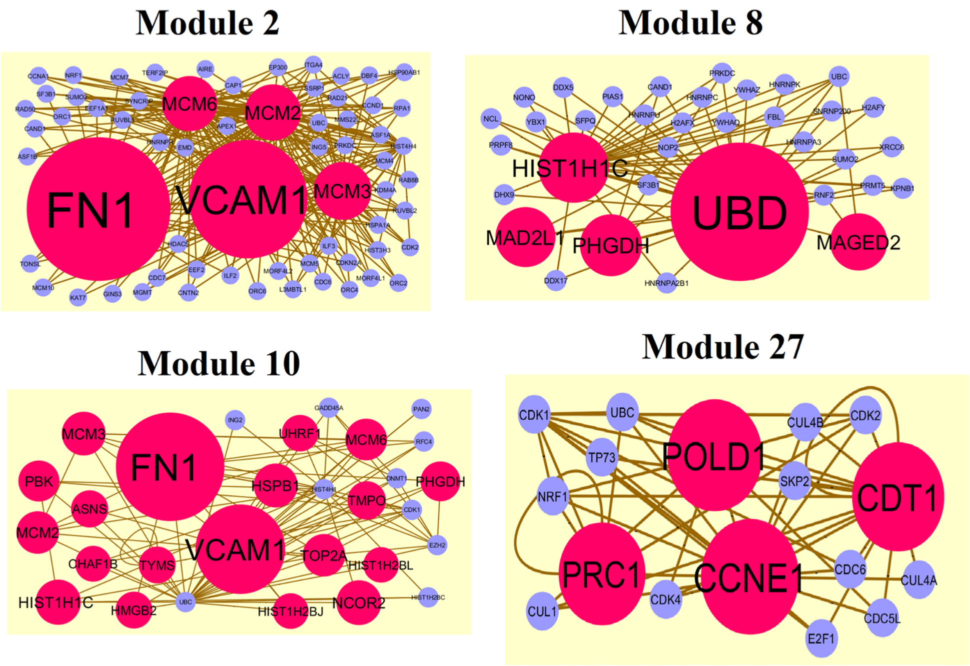


Fig. 11 Modules in PPI network. The pink round nodes denote down-regulated genes. Green dots are also genes which are not hub or differential expressed genes

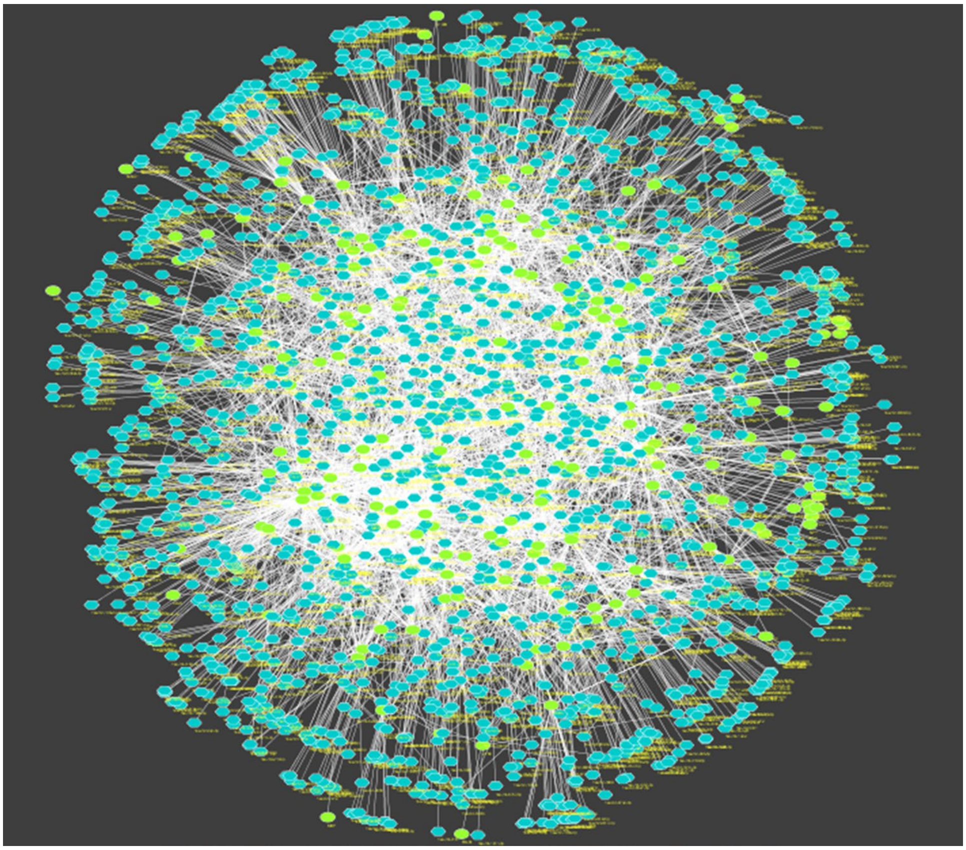


Fig. 12 The network of upregulated DEGs and their related miRNAs. The yellow circle nodes are the down-regulated target gene and blue diamond nodes are miRNAs. Black lines means interaction with adjutant genes or miRNAs

of gastroenteropancreatic neuroendocrine tumors [62], but this gene may be diagnosed with development of ACC. Genes such as FGF23 [63] and NEK3 [64] were liable for invasion of prostate cancer cells, but these genes may be associated with invasion of ACC cells. Single nucleotide polymorphism (SNP) in SLC2A4RG was linked with development of glioblastoma [65], but SNP in this gene may be liable for advancement of ACC. Alteration in CHTF18 was

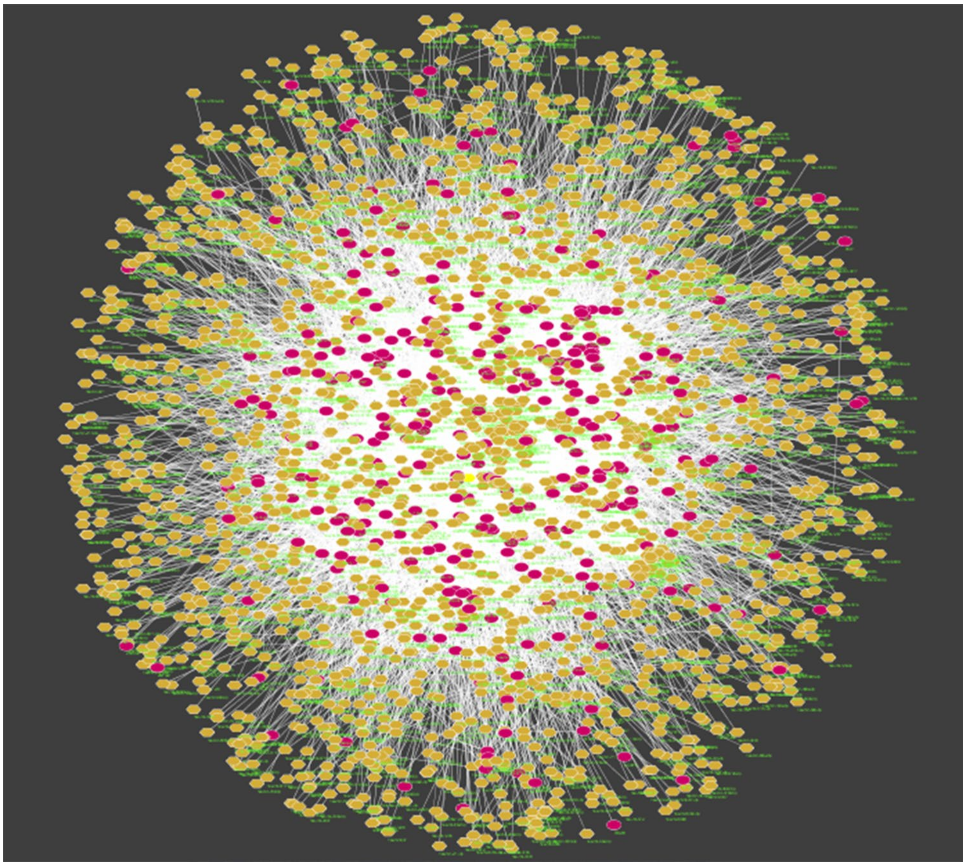


Fig. 13 The network of down-regulated DEGs and their related miRNAs. The red circle nodes are the down-regulated target gene and blue diamond nodes are miRNAs. Black lines means interaction with adjutant genes or miRNAs

linked with development of endometrial cancer [66], but mutation in this gene may be responsible for pathogenesis of ACC. HMGB2 was identified with development chemoresistance in gastric cancer [67], but this gene may be responsible for drug resistance in ACC. EZH2 was reasonable for pathogenesis of ACC [68].

In pathway enrichment analysis, up regulated genes were mainly associated with several pathways from different pathway databases (BIOCYC, KEGG, PID, REACTOME, GenMAPP, MSigDB C2 BIOCARTA, PantherDB, and SMPDB) such as catecholamine biosynthesis, aldosterone synthesis and secretion, IL6-mediated signaling events, metallothioneins bind metals, steroid hormone metabolism, ensemble of genes encoding extracellular matrix and extracellular matrix-associated proteins, dopamine receptor mediated signaling pathway, and leptin system. SNP in genes such as CYP11A1 [69], HSD3B1 [70], SCARB1 [71], lumican (LUM) [72], and IRS1 [73] were liable for progression of different cancers such as colorectal cancer, prostate cancer, thyroid cancer and breast cancer, but SNP in these genes may be involved in development of ACC. Gene such as CYP11B2 [74], HSD3B2 [75], STAT3 [76], CYP17A1 [77], CCN3 [78], IGFBP2 [79], IGFBP5 [80], IGFBP6 [80], and PRKAR2B [81] were diagnosed with growth of ACC. Genes such as MC2R [82], CCAAT/enhancer binding protein (C/EBP), beta (CEBPB) [83], and ANGPTL4 [84] were involved in proliferation of different cancer cells such as prostate cancer, breast cancer, and colorectal cancer, but these genes may be associated with proliferation of ACC cells. Gene such as NR4A1 [85], NR4A2 [86], PRKD3 [87], ADAMTS1 [88], CCL13 [89], CRLF1 [90], CXCL12 [91], CXCL2 [92], decorin (DCN) [93], FGF9 [94], GDF15 [95], plasminogen activator, tissue (PLAT) [96], S100A8 [97], S100A9 [97], SEMA6A [98], SRPX2 [99], and tenascin XB (TNXB) [100] were important for invasion of different cancer cells such as breast cancer, colorectal cancer, prostate cancer, thyroid cancer, ovarian cancer, endometrial cancer, gastric cancer, glioblastoma, and mesothelioma, but these genes may be linked with invasion of ACC cells. IL6 was responsible for inflammation in breast cancer [101], but this gene may be linked with inflammation in ACC. High expression of jun B proto-oncogene (JUNB) [102], STAT1 [103], MT1E [104], FGF7 [105], fibromodulin (FMOD) [106], SPON2 [107], and THBS1 [108] were important for advancement of different cancers such as renal cancer, colon cancer, breast cancer, prostate cancer and esophageal squamous cell carcinoma, but high expression of these genes may be identified with growth of ACC. Methylation inactivation of tumor suppressor genes such as SOCS3 [109], MT1G [110], MT1H [111], ADAMTS9 [112], ANGPTL1 [113],

Table 7 Target gene–miRNA interaction table

Regulation	Target gene	Degree	MicroRNA	Regulation	Target gene	Degree	MicroRNA
Up	YWHAZ	212	hsa-mir-3662	Down	TXNIP	228	hsa-mir-6845-5p
Up	GATA6	207	hsa-mir-4273	Down	MAPKAPK5	179	hsa-mir-548az-3p
Up	LDLR	167	hsa-mir-4666a-3p	Down	PMAIP1	147	hsa-mir-4316
Up	BZW1	149	hsa-mir-548u	Down	RAD51	147	hsa-mir-6722-3p
Up	IGFBP5	144	hsa-mir-5703	Down	MICA	142	hsa-mir-6808-5p
Up	HSPA4L	141	hsa-mir-6879-3p	Down	MRNIP	124	hsa-mir-4722-5p
Up	PEG10	138	hsa-mir-4443	Down	DYRK2	118	hsa-mir-3689a-3p
Up	PTP4A1	135	hsa-mir-548ad-5p	Down	FZD6	115	hsa-mir-2113
Up	MAT2A	112	hsa-mir-3689a-3p	Down	HIST1H2BD	112	hsa-mir-548bb-5p
Up	DNAJB9	99	hsa-mir-410-3p	Down	RACGAP1	112	hsa-mir-5698
Up	CPE	98	hsa-mir-6511a-5p	Down	HOXA13	111	hsa-mir-6837-3p
Up	THBS1	95	hsa-mir-4441	Down	CPM	111	hsa-mir-6771-5p
Up	KCNK5	95	hsa-mir-7977	Down	RRM2	101	hsa-mir-548ah-5p
Up	FOSL2	94	hsa-mir-1827	Down	RAB11FIP4	100	hsa-mir-208b-5p
Up	ATP1B3	89	hsa-mir-520 h	Down	NR3C1	100	hsa-mir-6849-3p
Up	FOXK2	84	hsa-mir-4743-3p	Down	ZWINT	98	hsa-mir-4421
Up	AS3MT	81	hsa-mir-5690	Down	COL1A1	97	hsa-mir-4779
Up	STAT3	80	hsa-mir-500b-3p	Down	TP53INP1	94	hsa-mir-6853-3p
Up	NDRG1	80	hsa-mir-512-3p	Down	HMGB2	89	hsa-mir-548az-5p
Up	UNC5B	79	hsa-mir-550a-3-5p	Down	VCAM1	86	hsa-mir-6884-5p
Up	ADM	77	hsa-mir-3121-3p	Down	IER5	85	hsa-mir-4659b-3p
Up	RAB21	72	hsa-mir-3126-3p	Down	CCNB1	84	hsa-mir-548am-5p
Up	NPTX1	69	hsa-mir-3145-5p	Down	CHST6	81	hsa-mir-5589-5p
Up	SLC16A9	69	hsa-mir-548p	Down	HMBOX1	81	hsa-mir-548ar-5p
Up	SF1	69	hsa-mir-4294	Down	MCM8	80	hsa-mir-4711-3p
Up	TGFBR3	67	hsa-mir-548ah-3p	Down	CHAF1B	79	hsa-mir-7703
Up	BHMT2	67	hsa-mir-4707-3p	Down	BIRC5	78	hsa-mir-4716-5p
Up	HOXA9	64	hsa-mir-548 m	Down	PDCD4	78	hsa-mir-6747-3p
Up	CREBL2	63	hsa-mir-548aw	Down	PSAT1	77	hsa-mir-548z
Up	MSI2	61	hsa-mir-6500-5p	Down	MELK	74	hsa-mir-4701-3p
Up	PDGFRA	61	hsa-mir-548aq-3p	Down	MYO10	74	hsa-mir-4524a-3p
Up	NRXN3	61	hsa-mir-4768-3p	Down	HIST1H2BJ	73	hsa-mir-5697
Up	CGNL1	61	hsa-mir-6884-5p	Down	BBC3	73	hsa-mir-4649-3p
Up	MC2R	59	hsa-mir-676-5p	Down	AHR	71	hsa-mir-3689b-3p
Up	SOAT1	57	hsa-mir-6893-5p	Down	ULK2	71	hsa-mir-6847-3p
Up	PGM3	56	hsa-mir-7844-5p	Down	ZBED3	67	hsa-mir-3650
Up	PSD3	56	hsa-mir-520e	Down	BUB1	67	hsa-mir-6878-5p
Up	SLC33A1	55	hsa-mir-508-5p	Down	HRK	66	hsa-mir-6755-5p
Up	CEBPB	54	hsa-mir-185-5p	Down	NCOR2	64	hsa-mir-6757-5p
Up	SH3BP5	54	hsa-mir-6504-3p	Down	CD3D	64	hsa-mir-6788-5p
Up	ELL2	54	hsa-mir-548av-3p	Down	GALNT10	64	hsa-mir-211-5p
Up	IPO7	53	hsa-mir-101-3p	Down	RHOBTB3	63	hsa-mir-3925-5p
Up	ZBED1	51	hsa-mir-520b	Down	ULK1	61	hsa-mir-4483
Up	ERN1	50	hsa-mir-4768-3p	Down	FANCA	60	hsa-mir-520a-3p
Up	NOLC1	49	hsa-mir-3529-3p	Down	TIMELESS	60	hsa-mir-2682-3p
Up	ZRANB1	48	hsa-mir-548f-3p	Down	RNF44	58	hsa-mir-16-2-3p
Up	SLC2A3	47	hsa-mir-6838-5p	Down	OGT	58	hsa-mir-4270
Up	CHSY1	47	hsa-mir-5197-5p	Down	MICB	56	hsa-mir-3689c
Up	FJX1	47	hsa-mir-5590-3p	Down	NOTCH2	55	hsa-mir-5100
Up	SLC1A2	47	hsa-mir-7977	Down	SRGAP2	50	hsa-mir-204-3p

Table 7 (continued)

Regulation	Target gene	Degree	MicroRNA	Regulation	Target gene	Degree	MicroRNA
Up	KCNK3	46	hsa-mir-4296	Down	CDT1	48	hsa-mir-550b-2-5p
Up	ARHGAP18	45	hsa-mir-4439	Down	SMS	48	hsa-mir-6511a-5p
Up	HOXA7	44	hsa-mir-3132	Down	E2F8	45	hsa-let-7f-2-3p
Up	EPB41L1	44	hsa-mir-4510	Down	MYBL2	45	hsa-mir-3184-5p
Up	DHCR24	43	hsa-mir-532-3p	Down	TK1	45	hsa-mir-6888-5p
Up	HSPA5	42	hsa-mir-5688	Down	EZH2	44	hsa-mir-3679-3p
Up	GABARAPL1	41	hsa-mir-6867-3p	Down	OIP5	44	hsa-mir-5690
Up	PLA2G4A	41	hsa-mir-2115-3p	Down	LRIG3	43	hsa-mir-7154-5p
Up	SERP1	41	hsa-mir-653-5p	Down	MAT1A	43	hsa-mir-5591-5p
Up	MT1A	41	hsa-mir-6749-3p	Down	HIST1H2BF	42	hsa-mir-22-5p
Up	SRPX2	40	hsa-mir-2052	Down	MUC20	42	hsa-mir-3664-3p
Up	IRS1	39	hsa-mir-4676-3p	Down	CABLES1	40	hsa-mir-548ae-3p
Up	FZD4	38	hsa-mir-4433a-3p	Down	MATN3	40	hsa-mir-6893-5p
Up	TFAP2B	38	hsa-mir-128-1-5p	Down	DDR1	40	hsa-mir-199a-5p
Up	DKK3	38	hsa-mir-6734-3p	Down	TRIM45	40	hsa-mir-548x-3p
Up	SERPING1	38	hsa-mir-519e-5p	Down	DNMT1	39	hsa-mir-377-3p
Up	SIRT1	37	hsa-mir-449b-5p	Down	TMEM44	39	hsa-mir-374b-3p
Up	PRKAR1A	37	hsa-mir-548az-5p	Down	TIGD2	39	hsa-mir-5197-5p
Up	HOXA5	35	hsa-mir-1909-5p	Down	PRSS8	38	hsa-mir-1203
Up	RAB34	34	hsa-mir-7113-5p	Down	TGFA	38	hsa-mir-5001-3p
Up	ICAM1	34	hsa-mir-4643	Down	CLDN1	35	hsa-mir-548u
Up	IER3	34	hsa-mir-7977	Down	NPTX2	35	hsa-mir-4300
Up	PRKD3	34	hsa-mir-4773	Down	CCNE1	34	hsa-mir-6838-5p
Up	CYB561	34	hsa-mir-548aj-5p	Down	WNT5A	32	hsa-mir-516a-3p
Up	PCK1	33	hsa-mir-3650	Down	OSBPL3	31	hsa-mir-6890-3p
Up	SOCS3	32	hsa-mir-8062	Down	UBD	31	hsa-mir-6886-3p
Up	LITAF	32	hsa-mir-548an	Down	HMGB3	30	hsa-mir-520 g-3p
Up	ALDH1A3	32	hsa-mir-4533	Down	KCNK1	30	hsa-mir-603
Up	RPRM	32	hsa-mir-6827-5p	Down	IQSEC1	29	hsa-mir-4436b-3p
Up	TAGLN	31	hsa-mir-9-5p	Down	TMPO	29	hsa-mir-409-3p
Up	ID2	31	hsa-mir-548t-5p	Down	JAG1	27	hsa-mir-4282
Up	GTPBP4	30	hsa-mir-6870-3p	Down	CDCA8	27	hsa-mir-6880-5p
Up	FGF9	29	hsa-mir-1279	Down	F11R	27	hsa-mir-6499-3p
Up	NR4A3	29	hsa-mir-4776-3p	Down	KNTC1	27	hsa-mir-5584-3p
Up	CEBPD	28	hsa-mir-6872-5p	Down	PTPN3	26	hsa-mir-4731-3p
Up	JUNB	28	hsa-mir-3960	Down	SLPI	26	hsa-mir-361-5p
Up	NKAIN1	28	hsa-mir-1255b-5p	Down	PPP1R13L	26	hsa-mir-9500
Up	CNN3	27	hsa-mir-888-5p	Down	ZNF443	25	hsa-mir-7856-5p
Up	ZNF331	27	hsa-mir-3187-5p	Down	KIT	25	hsa-mir-4504
Up	NEDD9	26	hsa-mir-5702	Down	GPX8	25	hsa-mir-6833-3p
Up	ECHDC3	26	hsa-mir-4717-5p	Down	TCEA3	24	hsa-mir-1233-3p
Up	PON1	26	hsa-mir-1273 g-3p	Down	HIST1H2BO	24	hsa-mir-8057
Up	QPCT	25	hsa-mir-7703	Down	DDX3Y	23	hsa-mir-548at-5p
Up	DNAJC3	24	hsa-mir-548av-5p	Down	POPDC2	23	hsa-mir-612
Up	TPMT	24	hsa-mir-5089-5p	Down	SLC2A4RG	23	hsa-mir-6787-5p
Up	GEM	24	hsa-mir-5093	Down	HIST1H1C	22	hsa-mir-3940-5p
Up	ADAMTS9	24	hsa-mir-548ah-5p	Down	CDCA7	22	hsa-mir-3606-3p
Up	CDH2	24	hsa-mir-208b-5p	Down	DMTF1	22	hsa-mir-644a
Up	STARD13	24	hsa-mir-219a-1-3p	Down	ZNF618	22	hsa-mir-548 s
Up	SAA1	24	hsa-mir-4651	Down	CDH1	22	hsa-mir-203a-3p

Table 7 (continued)

Regulation	Target gene	Degree	MicroRNA	Regulation	Target gene	Degree	MicroRNA
Up	ADH1B	24	hsa-mir-300	Down	PRSS16	22	hsa-mir-3135b
Up	VASN	23	hsa-mir-4254	Down	SERPINA3	22	hsa-mir-6500-3p
Up	SNAI1	23	hsa-mir-506-3p	Down	APOBEC3A	22	hsa-mir-212-5p
Up	SEMA6A	23	hsa-mir-506-3p	Down	ZSWIM9	22	hsa-mir-208a-5p
Up	FDX1	23	hsa-mir-3653-5p	Down	MMP9	21	hsa-mir-211-5p
Up	GDF15	23	hsa-mir-3681-3p	Down	GMNN	21	hsa-mir-7847-3p
Up	SPON2	23	hsa-mir-3150a-3p	Down	FGG	21	hsa-mir-6780b-3p
Up	IL6	22	hsa-let-7f-5p	Down	SPARC	21	hsa-mir-767-5p
Up	HAND2	22	hsa-mir-7111-5p	Down	PTCD1	20	hsa-mir-5580-5p
Up	SFPQ	22	hsa-mir-1229-3p	Down	DAND5	20	hsa-mir-7703
Up	CYP26B1	21	hsa-mir-4524a-5p	Down	PLXDC1	20	hsa-mir-3121-3p
Up	GJA1	21	hsa-mir-200a-3p	Down	CCDC14	19	hsa-mir-4302
Up	MT1E	21	hsa-mir-4677-5p	Down	TBC1D8	19	hsa-mir-7849-3p
Up	DUSP5	21	hsa-mir-16-1-3p	Down	DONSON	19	hsa-mir-5089-3p
Up	FRMD5	21	hsa-mir-548bb-3p	Down	HIST1H2BE	19	hsa-mir-299-5p
Up	CYP11A1	21	hsa-mir-4709-3p	Down	RFC5	19	hsa-mir-188-3p
Up	FGF7	20	hsa-mir-302d-3p	Down	HIST1H2BN	19	hsa-mir-4252
Up	MAP3K5	20	hsa-mir-642b-3p	Down	CDKN3	18	hsa-mir-1307-3p
Up	CXCL12	20	hsa-mir-7152-3p	Down	HIST1H2BB	18	hsa-mir-3940-5p
Up	STAT1	19	hsa-mir-1183	Down	CKAP2	17	hsa-mir-3609
Up	CREM	18	hsa-mir-3117-3p	Down	TOP2A	17	hsa-mir-5688
Up	GCLM	18	hsa-mir-6131	Down	MAD2L1	17	hsa-mir-3978
Up	PAPSS2	18	hsa-mir-297	Down	PHGDH	17	hsa-mir-6792-5p
Up	CTH	18	hsa-mir-4470	Down	PRC1	17	hsa-mir-5692a
Up	TIPARP	18	hsa-mir-4680-5p	Down	HIST1H2BL	17	hsa-mir-6839-3p
Up	MRAS	18	hsa-mir-2392	Down	CYP3A5	17	hsa-mir-3690
Up	ACVR1C	17	hsa-mir-376b-3p	Down	ANKRD23	17	hsa-mir-3960
Up	CRLF1	17	hsa-mir-377-3p	Down	IDH2	16	hsa-mir-1250-3p
Up	MTSS1	17	hsa-mir-6769b-3p	Down	ANGPTL2	15	hsa-mir-4789-5p
Up	GPM6B	16	hsa-mir-3919	Down	GADD45A	15	hsa-mir-135b-3p
Up	FUBP1	16	hsa-mir-222-3p	Down	NEK3	15	hsa-mir-548e-3p
Up	NR4A2	16	hsa-mir-520f-5p	Down	HIST1H4H	15	hsa-mir-4796-3p
Up	FBLN5	16	hsa-mir-200c-3p	Down	FABP3	15	hsa-mir-3907
Up	AOC3	16	hsa-mir-6800-5p	Down	UHRF1	14	hsa-mir-191-5p
Up	P2RY2	16	hsa-mir-6511a-3p	Down	ZNF606	14	hsa-mir-653-3p
Up	GALC	15	hsa-mir-3606-3p	Down	SMYD2	14	hsa-mir-5588-3p
Up	SYT4	15	hsa-mir-106b-5p	Down	DNMT3B	14	hsa-mir-506-3p
Up	RASD1	15	hsa-mir-3180	Down	MCM3	14	hsa-mir-1260b
Up	CD38	15	hsa-mir-4659a-5p	Down	HIST1H2BH	14	hsa-mir-5693
Up	SCARB1	14	hsa-mir-3121-5p	Down	TYMS	13	hsa-mir-99a-5p
Up	ADAMTS1	13	hsa-mir-6854-3p	Down	KIF11	13	hsa-mir-340-5p
Up	HES1	12	hsa-mir-765	Down	ZNF266	13	hsa-mir-4262
Up	ENPP2	12	hsa-mir-17-3p	Down	CHAF1A	12	hsa-mir-20b-5p
Up	ABCB1	12	hsa-mir-508-5p	Down	CENPF	12	hsa-mir-122-5p
Up	HSPA1A	11	hsa-mir-223-5p	Down	IGFBP3	12	hsa-mir-210-3p
Up	NBEA	11	hsa-mir-18a-5p	Down	COL4A5	12	hsa-mir-802
Up	SCN7A	11	hsa-mir-3675-3p	Down	PNMA3	12	hsa-mir-6792-3p
Up	XBP1	10	hsa-mir-320c	Down	COL14A1	12	hsa-mir-548an
Up	CCL2	10	hsa-let-7 g-3p	Down	COL3A1	11	hsa-mir-29b-1-5p
Up	C1S	10	hsa-mir-4778-3p	Down	RPS4Y1	11	hsa-mir-208b-3p

Table 7 (continued)

Regulation	Target gene	Degree	MicroRNA	Regulation	Target gene	Degree	MicroRNA
Up	TMEM130	10	hsa-mir-644a	Down	PLK2	11	hsa-mir-190a-3p
Up	PHOX2B	10	hsa-mir-181d-5p	Down	ZDHHC23	11	hsa-mir-4668-3p
Up	GNAZ	10	hsa-mir-5587-5p	Down	SULF2	11	hsa-mir-4439
Up	AADAC	10	hsa-mir-8062	Down	RAD51AP1	10	hsa-mir-18b-5p
Up	LRRC38	10	hsa-mir-1228-3p	Down	KIAA1324L	10	hsa-mir-6832-3p
Up	C7	10	hsa-mir-1245b-3p	Down	MCM2	10	hsa-mir-500a-5p
Up	CYP11B2	9	hsa-mir-4666b	Down	FHOD1	10	hsa-mir-4789-3p
Up	HSD3B1	9	hsa-mir-500a-5p	Down	MYO5C	10	hsa-mir-6512-3p
Up	FGF23	9	hsa-mir-548az-5p	Down	BARD1	10	hsa-mir-6501-3p
Up	DUSP16	9	hsa-mir-892a	Down	ENC1	10	hsa-mir-505-5p
Up	RND3	8	hsa-mir-200b-3p	Down	HOMER1	9	hsa-mir-5010-3p
Up	FCN2	8	hsa-mir-5589-3p	Down	PPP1R13B	9	hsa-mir-29c-3p
Up	EGR1	8	hsa-mir-181a-5p	Down	GRAMD1C	9	hsa-mir-3200-5p
Up	CASP9	7	hsa-let-7a-5p	Down	PTTG1	8	hsa-mir-146a-3p
Up	PHF10	7	hsa-mir-409-3p	Down	XYLT2	8	hsa-mir-18a-5p
Up	S100A9	7	hsa-mir-1204	Down	MSH2	8	hsa-mir-15a-5p
Up	SNAPC1	7	hsa-mir-4742-3p	Down	HIST1H2BC	8	hsa-mir-296-3p
Up	NR4A1	6	hsa-let-7d-5p	Down	NCOA6	8	hsa-mir-33a-5p
Up	CTSD	6	hsa-mir-339-5p	Down	ROR1	8	hsa-mir-3922-3p
Up	PDK4	6	hsa-mir-103a-3p	Down	FN1	8	hsa-mir-200c-3p
Up	KCTD14	6	hsa-mir-27a-3p	Down	RNFT2	8	hsa-mir-922
Up	GRK5	6	hsa-mir-1238-5p	Down	IQGAP2	8	hsa-mir-208a-3p
Up	CALD1	5	hsa-mir-15a-5p	Down	ANXA4	8	hsa-mir-7161-5p
Up	TBX3	5	hsa-mir-206	Down	XRCC1	8	hsa-mir-5700
Up	UCHL1	5	hsa-mir-218-5p	Down	COL27A1	8	hsa-mir-6757-5p
Up	CXCL2	5	hsa-mir-532-5p	Down	CCDC74A	8	hsa-mir-411-3p
Up	SYT13	5	hsa-mir-6743-5p	Down	STK36	8	hsa-mir-8485
Up	HEPH	5	hsa-mir-3613-3p	Down	ASNS	7	hsa-mir-17-5p
Up	SLC25A19	4	hsa-let-7b-5p	Down	COL5A2	7	hsa-mir-222-3p
Up	HOXB2	4	hsa-mir-4762-5p	Down	HPGD	7	hsa-mir-664a-3p
Up	ABR	4	hsa-mir-93-3p	Down	TTK	7	hsa-mir-376a-5p
Up	FGF12	4	hsa-mir-4668-5p	Down	OSBPL6	7	hsa-mir-4477b
Up	TNFRSF11B	4	hsa-mir-181b-5p	Down	NEK2	7	hsa-mir-4668-5p
Up	TESK1	4	hsa-mir-32-5p	Down	FBXO32	7	hsa-mir-4647
Up	ATP5L	4	hsa-mir-100-5p	Down	ESM1	7	hsa-mir-1260a
Up	ANGPTL4	4	hsa-mir-29b-3p	Down	ASPM	6	hsa-let-7a-5p
Up	CD83	4	hsa-mir-373-3p	Down	POLD1	6	hsa-let-7e-5p
Up	SCAP	4	hsa-mir-10a-5p	Down	LAMB1	6	hsa-mir-760
Up	IGFBP2	4	hsa-mir-204-5p	Down	HCP5	6	hsa-mir-519d-3p
Up	TMEM25	4	hsa-mir-636	Down	RAI14	6	hsa-mir-423-3p
Up	TMOD1	4	hsa-mir-1185-1-3p	Down	KIF22	6	hsa-mir-25-5p
Up	NPC1	3	hsa-mir-33a-5p	Down	MCM6	6	hsa-mir-1180-3p
Up	RAB38	3	hsa-mir-30a-5p	Down	CD99L2	6	hsa-mir-3064-3p
Up	PLAT	3	hsa-mir-21-5p	Down	CDCA2	6	hsa-mir-5586-5p
Up	PTX3	3	hsa-mir-224-5p	Down	SUCNR1	6	hsa-mir-4501
Up	S100A8	3	hsa-mir-125b-5p	Down	CCNB2	5	hsa-let-7f-5p
Up	NFIL3	3	hsa-mir-183-5p	Down	TCFL5	5	hsa-mir-331-3p
Up	MT1F	3	hsa-mir-219a-5p	Down	ANKRA2	5	hsa-mir-30a-5p
Up	APOE	3	hsa-mir-1908-5p	Down	CCNG2	5	hsa-mir-93-3p
Up	SDF2L1	3	hsa-mir-30c-5p	Down	HMMR	5	hsa-mir-98-5p

Table 7 (continued)

Regulation	Target gene	Degree	MicroRNA	Regulation	Target gene	Degree	MicroRNA
Up	ALDH3A2	3	hsa-mir-155-5p	Down	EML1	5	hsa-mir-1229-3p
Up	AKR1B1	3	hsa-mir-342-5p	Down	ANLN	5	hsa-mir-503-5p
Up	DLL1	3	hsa-mir-130b-3p	Down	KIF24	5	hsa-mir-7-5p
Up	CXCL1	3	hsa-mir-27b-5p	Down	BMF	5	hsa-mir-34c-5p
Up	NEFH	3	hsa-mir-142-3p	Down	RALGDS	5	hsa-mir-374a-5p
Up	IFI27	3	hsa-mir-502-5p	Down	SPAG5	5	hsa-mir-539-5p
Up	FMOD	2	hsa-mir-124-3p	Down	PBK	5	hsa-mir-216b-5p
Up	SLC27A6	2	hsa-mir-26b-5p	Down	PCYOX1L	5	hsa-mir-5002-3p
Up	PDE8A	2	hsa-mir-33a-5p	Down	NTN4	4	hsa-mir-196a-5p
Up	MGST1	2	hsa-mir-652-3p	Down	GUSB	4	hsa-mir-449b-3p
Up	MT1X	2	hsa-mir-1225-3p	Down	CD69	4	hsa-mir-32-5p
Up	FNDC4	2	hsa-mir-7-5p	Down	CDCA5	3	hsa-mir-18b-5p
Up	GK	2	hsa-mir-132-3p	Down	FANCG	3	hsa-mir-744-5p
Up	ALDH1A1	2	hsa-mir-140-5p	Down	BRD8	3	hsa-mir-24-3p
Up	NR2F1	2	hsa-mir-181b-5p	Down	DDB2	3	hsa-mir-675-5p
Up	TCEAL7	2	hsa-mir-182-5p	Down	LIG1	3	hsa-mir-149-5p
Up	MFAP4	2	hsa-mir-449a	Down	CXCL9	3	hsa-mir-26b-5p
Up	PLEK2	2	hsa-mir-138-5p	Down	HSPB7	3	hsa-mir-124-3p
Up	PC	2	hsa-mir-125a-5p	Down	THOC3	3	hsa-mir-27a-3p
Up	MAPK4	2	hsa-mir-127-3p	Down	FUK	3	hsa-mir-92a-3p
Up	ABTB2	2	hsa-mir-106b-5p	Down	ADA	3	hsa-mir-140-5p
Up	DLG2	2	hsa-mir-148b-3p	Down	RFC4	3	hsa-mir-193b-3p
Up	ALAS1	2	hsa-mir-423-3p	Down	ERICH5	3	hsa-mir-215-5p
Up	AASS	2	hsa-mir-591	Down	ANGPT2	3	hsa-mir-542-3p
Up	GPRASP1	2	hsa-mir-3140-3p	Down	LGALS3	3	hsa-mir-744-5p
Up	CDH18	1	hsa-let-7e-5p	Down	CCL19	3	hsa-mir-9-5p
Up	AOX1	1	hsa-mir-26b-5p	Down	EXO1	3	hsa-mir-30e-5p
Up	FMO3	1	hsa-mir-26b-5p	Down	CHTF18	3	hsa-mir-378a-5p
Up	GSTT2	1	hsa-mir-26b-5p	Down	HHEX	2	hsa-mir-19b-3p
Up	PNMT	1	hsa-mir-26b-5p	Down	SULT2A1	2	hsa-mir-24-3p
Up	IL1R2	1	hsa-mir-26b-5p	Down	HIST1H4J	2	hsa-mir-26a-5p
Up	CH25H	1	hsa-mir-26b-5p	Down	DFNA5	2	hsa-mir-1-3p
Up	IL1RL1	1	hsa-mir-26b-5p	Down	LAMA3	2	hsa-mir-181a-5p
Up	DNAJC12	1	hsa-mir-26b-5p	Down	HIST1H2BI	2	hsa-mir-98-5p
Up	FBLN1	1	hsa-mir-30a-3p	Down	PAQR6	2	hsa-mir-335-5p
Up	HBB	1	hsa-mir-92a-3p	Down	PAQR4	2	hsa-mir-96-5p
Up	LXN	1	hsa-mir-92a-3p	Down	KIF18A	2	hsa-mir-192-5p
Up	SCG2	1	hsa-mir-98-5p	Down	CCDC150	2	hsa-mir-215-5p
Up	CHGA	1	hsa-mir-107	Down	ZNF700	2	hsa-mir-425-5p
Up	MGAT2	1	hsa-mir-30c-5p	Down	RHOBTB2	2	hsa-mir-106b-5p
Up	SLCO2A1	1	hsa-mir-181a-5p	Down	PNLIPRP2	2	hsa-mir-148b-3p
Up	TH	1	hsa-mir-1-3p	Down	MAGED2	2	hsa-mir-877-3p
Up	RGN	1	hsa-mir-1-3p	Down	POSTN	1	hsa-let-7f-5p
Up	PI16	1	hsa-mir-1-3p	Down	GRB14	1	hsa-mir-26b-5p
Up	ECE2	1	hsa-mir-124-3p	Down	SPRR1A	1	hsa-mir-26b-5p
Up	CLDN5	1	hsa-mir-128-3p	Down	ZNF133	1	hsa-mir-26b-5p
Up	ADH1A	1	hsa-mir-132-3p	Down	RAD54L	1	hsa-mir-26b-5p
Up	KCNQ1	1	hsa-mir-133a-3p	Down	LY6D	1	hsa-mir-26b-5p
Up	CRH	1	hsa-mir-142-3p	Down	GGH	1	hsa-mir-26b-5p
Up	DDC	1	hsa-mir-145-5p	Down	NUP107	1	hsa-mir-93-5p

Table 7 (continued)

Regulation	Target gene	Degree	MicroRNA	Regulation	Target gene	Degree	MicroRNA
Up	GSTA4	1	hsa-mir-185-5p	Down	PLAGL1	1	hsa-mir-98-5p
Up	CHGB	1	hsa-mir-375	Down	PALMD	1	hsa-mir-98-5p
Up	AQP11	1	hsa-mir-375	Down	ZNF302	1	hsa-mir-197-3p
Up	NAP1L5	1	hsa-mir-381-3p	Down	TAF1C	1	hsa-mir-30d-5p
Up	APOC1	1	hsa-mir-335-5p	Down	HIST1H4F	1	hsa-mir-34a-5p
Up	CYP21A2	1	hsa-mir-335-5p	Down	HIST1H4K	1	hsa-mir-34a-5p
Up	DBH	1	hsa-mir-335-5p	Down	DEPDC7	1	hsa-mir-132-3p
Up	HSD3B2	1	hsa-mir-335-5p	Down	LCN2	1	hsa-mir-138-5p
Up	NPY	1	hsa-mir-335-5p	Down	NUDT1	1	hsa-mir-145-5p
Up	NPY1R	1	hsa-mir-335-5p	Down	RANBP17	1	hsa-mir-361-5p
Up	RARRES2	1	hsa-mir-335-5p	Down	ZNF404	1	hsa-mir-375
Up	SEMA3B	1	hsa-mir-335-5p	Down	RABEP2	1	hsa-mir-378a-3p
Up	CDH19	1	hsa-mir-335-5p	Down	PDE8B	1	hsa-mir-335-5p
Up	SCG3	1	hsa-mir-335-5p	Down	ZG16B	1	hsa-mir-335-5p
Up	GIPC2	1	hsa-mir-335-5p	Down	CCDC112	1	hsa-mir-335-5p
Up	AK7	1	hsa-mir-335-5p	Down	OR8U1	1	hsa-mir-146b-5p
Up	STARD6	1	hsa-mir-335-5p	Down	ITPKA	1	hsa-mir-193b-3p
Up	ARHGAP36	1	hsa-mir-335-5p	Down	APOBEC3B	1	hsa-mir-193b-3p
Up	ARFGAP3	1	hsa-mir-93-3p	Down	TPX2	1	hsa-mir-193b-3p
Up	EFEMP1	1	hsa-mir-338-5p	Down	NR0B1	1	hsa-mir-561-3p
Up	PRKAR2B	1	hsa-mir-590-3p	Down	CAP2	1	hsa-mir-605-5p
Up	ANGPTL1	1	hsa-mir-921	Down	CX3CR1	1	hsa-mir-296-3p
Up	TNXB	1	hsa-mir-1301-3p	Down	DEF6	1	hsa-mir-3662
Up	ATP4A	1	hsa-mir-1289				

Degree—no of miRNA interact with target gene. We taken any one miRNA in table

FBLN1 [114], FCN2 [115], SEMA3B [116], and TIMP4 [117] were diagnosed with growth of different cancers such as prostate cancer, gastric cancer hepatocellular carcinoma, and lung cancer, but loss of these genes may be responsible for pathogenesis of ACC. Decrease expression of tumor suppressor gene MT1F was liable for progression of hepatocellular carcinoma [118], but less expression of this gene may be identified with growth of ACC. Genes such as CCL2 [119], CXCL1 [120], and EFEMP1 [121] were associated with angiogenesis in different cancers such as breast cancer and colorectal cancer, but these genes may be linked with angiogenesis in ACC. Tyrosine hydroxylase (TH) [122] and neuropeptide Y (NPY) [123] were responsible for pathogenesis of pheochromocytoma, but these genes may be associated with development of ACC. Dopa decarboxylase (aromatic L-amino acid decarboxylase) (DDC), CYP21A2, KCNK3, low density lipoprotein receptor (LDLR), CCAAT/enhancer binding protein (C/EBP), delta (CEBPD), MT1A, MT1B, MT1X, CTSD, FBLN5, FGF12, MFAP4, SERPING1, SPOCK3, dopamine beta-hydroxylase (dopamine beta-monooxygenase) (DBH) EPB41L1 and guanine nucleotide binding protein (G protein), alpha z polypeptide (GNAZ) were novel biomarkers for pathogenesis of ACC in these pathways. Meanwhile down regulated genes were mainly associated with several pathways from different pathway databases such as pyrimidine deoxyribonucleosides salvage, systemic lupus erythematosus, FOXM1 transcription factor network, SIRT1 negatively regulates rRNA expression, methionine metabolism, CDK regulation of DNA replication, integrin signaling pathway, mismatch repair pathway, and adenosine deaminase deficiency. High expression of genes such as TK1 [124], thymidylatesynthetase (TYMS) [125], CCNE1 [126], CDT1 [127], FN1 [128], NTN4 [129], and adenosine deaminase (ADA) [130] were associated with pathogenesis of different cancer such as breast cancer, colorectal cancer, ovarian cancer, and prostate cancer, but elevated expression of these genes may be liable for development of ACC. Genes such as HLA-DQB1 [131], MCM2 [132], and MSH2 [133] were involved in pathogenesis of ACC. Metylation inactivation of tumor suppressor gene DNMT1 was responsible for progression of colon cancer [134], but loss of this gene may be associated with pathogenesis of ACC. Genes such as MCM3 [135] and MCM6 [136] were associated with proliferation of different cancer cells such as ovarian cancer and lung cancer, but these genes may be liable for advancement of ACC. Genes such as COL1A1

Table 8 Target gene–miRNA interaction table

Regulation	TF	Degree	Target gene	Regulation	TF	Degree	Target gene
Up	TFDP1	67	HSPA1A	Down	TFDP1	78	F11R
Up	EZH2	54	PHOX2B	Down	GTF2E2	69	CHAF1B
Up	MAZ	52	H19	Down	KLF9	62	FANCG
Up	MXD4	51	CEBPD	Down	ELF1	61	CENPF
Up	KDM5B	50	DNAJC3	Down	ZNF580	61	XRCC1
Up	PHF8	50	HOXA7	Down	MXD3	60	IQGAP2
Up	KLF9	50	KCTD14	Down	SMAD5	60	MAPKAPK5
Up	SAP30	50	TIPARP	Down	IRF1	60	RRM2
Up	NR2F6	46	HES1	Down	ZNF24	60	ST6GALNAC2
Up	SOX13	45	BZW1	Down	PHF8	59	CHTF18
Up	ZNF580	45	LDLR	Down	KDM5B	59	NR3C1
Up	HBP1	44	DDC	Down	SAP30	59	TMPO
Up	TGIF2	42	GK	Down	SIN3A	58	HOXA13
Up	XBP1	42	TCF7	Down	CREB3L1	58	PLA2G1B
Up	MXD3	42	XBP1	Down	ATF1	57	TP53INP1
Up	ZBTB33	41	HOXA9	Down	ZNF76	56	C14orf80
Up	SIN3A	41	HOXB2	Down	ZBTB26	56	HCP5
Up	ZNF423	40	CNN3	Down	ZBTB11	55	MAT1A
Up	ZNF24	40	GSTA4	Down	ZFX	54	RAD54L
Up	ATF3	40	MT1F	Down	NR2F6	54	TYMS
Up	CHD1	40	YWHAZ	Down	POLR2A	53	CHAF1A
Up	SSRP1	39	NFIL3	Down	ZNF501	51	BIRC5
Up	ZNF501	38	DLL1	Down	KLF16	51	FN1
Up	RXRB	38	GABARAPL1	Down	MAZ	50	LAMA3
Up	KLF11	38	HSPA5	Down	DMAP1	49	BTBD11
Up	SUZ12	37	TFAP2B	Down	ZFP2	49	DDR1
Up	ZNF76	36	CITED1	Down	TAF7	49	HMMR
Up	ATF1	36	CRLF1	Down	MBD1	47	DEF6
Up	IRF1	36	IL6	Down	ZNF324	46	DONSON
Up	ZBTB11	36	STAT3	Down	NR4A1	45	CX3CR1
Up	GATAD1	35	MT1B	Down	NRF1	45	NRF1
Up	ZBTB26	35	SELK	Down	ETV4	45	SULT2A1
Up	CTBP2	35	NOLC1	Down	ZFP37	44	CABLES1
Up	NRF1	34	AK7	Down	FOXJ2	44	CDCA5
Up	ETV4	34	APOE	Down	CBFB	44	DEPDC7
Up	HIC1	34	CNN1	Down	SP1	44	PRSS8
Up	RAD21	34	EPB41L1	Down	ELK1	44	THOC3
Up	ZNF324	34	PAPSS2	Down	GABPA	44	ZNF302
Up	KLF16	34	TMEM25	Down	KLF1	43	LRIG3
Up	YY1	33	CTH	Down	ZNF644	43	NUP107
Up	HMG20B	33	NEDD9	Down	CHD1	43	PHGDH
Up	ZFX	33	UNC5B	Down	PPARG	43	RACGAP1
Up	IRF4	32	CD83	Down	NCOR1	43	TXNIP
Up	FOXM1	32	CYB561	Down	MXD4	41	COL27A1
Up	ZNF341	32	DUSP5	Down	BCL6	41	IDH2
Up	BCL11A	32	EGR1	Down	KLF11	41	KIF22
Up	ELF1	32	GDF15	Down	HDGF	41	LTB
Up	MLLT1	32	IPO7	Down	ETS1	41	MXD4
Up	THRB	32	PCK1	Down	MLLT1	40	ADA
Up	BCL11B	32	RAB34	Down	MYNN	40	BBC3
Up	CEBPG	32	S100A9	Down	ZFP64	40	BMF

Table 8 (continued)

Regulation	TF	Degree	Target gene	Regulation	TF	Degree	Target gene
Up	ZBTB7A	32	TGFBR3	Down	WT1	40	MCM3
Up	ZFP2	31	DNER	Down	ZBTB7A	40	RHOBTB3
Up	KLF8	30	FJX1	Down	NR2C2	40	XYLT2
Up	GATA4	30	ID2	Down	MLX	39	DAND5
Up	DMAP1	30	LITAF	Down	ZNF589	39	GMNN
Up	ZFP64	30	PTP4A1	Down	NFRKB	39	ZNF700
Up	TFE3	30	SCARB1	Down	ZNF71	38	CCNE1
Up	CTCF	30	SLC27A6	Down	HBP1	38	CDH1
Up	BCL6	29	C7	Down	HMG20B	38	DPP4
Up	ZNF589	29	G0S2	Down	ZNF2	38	HOMER1
Up	ZNF71	29	PDK4	Down	GTF2F1	38	KIAA0101
Up	HMGN3	29	TMOD1	Down	HMGN3	38	NUDT1
Up	MYNN	28	ALDH3A2	Down	DDX20	38	TTK
Up	FOXA3	28	ATP1B3	Down	FOSL1	37	ANLN
Up	RARA	28	BZW1	Down	REST	37	ANXA4
Up	FOSL1	28	CALD1	Down	ARID4B	37	CABLES1
Up	NR2C2	28	CXCL2	Down	RERE	37	CDCA5
Up	MLX	28	FOXK2	Down	RFXANK	37	HLA-DQB1
Up	SP3	28	GJA1	Down	TFE3	37	LCN2
Up	ZNF610	28	PLAT	Down	ZNF197	37	NEK2
Up	RCOR2	28	SNAI1	Down	KDM5A	37	OIP5
Up	SP2	27	AS3MT	Down	SOX13	37	TAF1C
Up	RERE	27	DHCR24	Down	ZNF394	36	BARD1
Up	REST	27	ECE2	Down	SSRP1	36	FGG
Up	MBD1	27	EPB41L1	Down	ZBTB40	36	MSH2
Up	TRIM28	27	FGF9	Down	ELF3	36	NCOA6
Up	ZNF197	27	FUBP1	Down	TGIF2	36	RFC4
Up	DRAP1	27	ICAM1	Down	HMG20A	36	SERPINA3
Up	ZFP37	27	MAT2A	Down	POLR2H	35	CD69
Up	SMAD4	27	MT1E	Down	INSM2	35	GADD45A
Up	GLIS2	27	SF1	Down	E2F4	35	MAD2L1
Up	GATA2	26	CHGA	Down	NR2F1	35	PCYOX1L
Up	ZEB1	26	SCG3	Down	KLF13	35	POLD1
Up	HNF4G	25	C1S	Down	ZBTB33	35	PPP1R13B
Up	ZNF2	25	HOXA5	Down	ID3	35	SUCNR1
Up	ELF3	25	HP	Down	ZNF610	35	TIGD2
Up	ARID4B	25	IER3	Down	NFIL3	34	GGH
Up	GTF2F1	25	JUNB	Down	NCOA1	34	HIST1H2BH
Up	ZNF394	25	MAPK4	Down	NFYC	34	HIST1H4J
Up	MYBL2	25	MT1H	Down	RXRB	34	ITPKA
Up	KLF7	25	NPC1	Down	CREB1	34	LAMB1
Up	NFIA	25	PEG10	Down	CREM	34	UHRF1
Up	MBD4	25	RAMP1	Down	GLIS2	33	APOBEC3A
Up	INSM2	25	SOCS3	Down	MEF2D	33	HIST1H1C
Up	SOX5	25	TESK1	Down	LEF1	33	HIST1H2BE
Up	TEAD3	25	VASN	Down	ADNP	33	HIST1H2BL
Up	NFRKB	24	ANGPTL4	Down	WRNIP1	33	HIST1H4F
Up	ZHX2	24	AOC3	Down	ETV1	33	HIST1H4K
Up	NCOR1	24	HBB	Down	GATAD1	32	CSRP2BP
Up	POLR2A	24	HEPH	Down	IKZF1	32	CYP3A7
Up	PPARG	24	MSI2	Down	GATA4	32	HIST1H2BB

Table 8 (continued)

Regulation	TF	Degree	Target gene	Regulation	TF	Degree	Target gene
Up	L3MBTL2	24	NPTX1	Down	ZEB1	32	HIST1H2BF
Up	KDM1A	24	TLX2	Down	BCL11B	32	HIST1H2BI
Up	GTF2E2	24	G0S2	Down	KDM1A	32	HIST1H2BN
Up	RFXANK	23	STAT3	Down	SP3	31	AHR
Up	CREB3L1	23	CHSY1	Down	KLF6	31	HIST1H2BC
Up	TAF7	23	RARRES2	Down	RCOR2	31	HIST1H2BD
Up	KLF1	22	GNAZ	Down	KLF8	31	HIST1H4H
Up	WT1	22	NR2F1	Down	SUPT5H	31	MUC20
Up	E2F5	22	ANGPTL4	Down	ZNF423	31	OSBPL6
Up	SMARCA5	22	PLAT	Down	HIC1	31	SMS
Up	TFAP4	22	SEMA3B	Down	L3MBTL2	31	WNT5A
Up	SMARCE1	22	TPMT	Down	THRB	30	CDCA7
Up	GABPA	22	STARD6	Down	FOXM1	30	FUK
Up	NFYC	22	MAT2A	Down	EGR1	30	HSPB1
Up	BHLHE40	22	PDGFRA	Down	BCL11A	30	KIF22
Up	ZNF101	21	CH25H	Down	CEBPG	30	MCM8
Up	BCOR	21	SPON2	Down	MBD2	30	MSH2
Up	ETS1	21	MGAT2	Down	KLF7	30	PCYOX1L
Up	ESRRA	21	CCL13	Down	CCNT2	30	RALGDS
Up	SP1	21	AQP11	Down	ESRRA	30	RFC5
Up	WRNIP1	21	SLC2A3	Down	IRF4	30	ZG16B
Up	DPF2	21	SLC33A1	Down	ZKSCAN1	30	ZKSCAN1
Up	ELK1	21	RAB34	Down	ZNF101	29	ROR1
Up	HDGF	20	SLC25A19	Down	BACH1	29	ANKRA2
Up	ZNF644	20	PCK1	Down	MIXL1	29	RHOBTB3
Up	CREB1	20	QPCT	Down	E2F5	29	PAQR4
Up	MBD2	20	CREBL2	Down	SMARCA5	29	SMARCA5
Up	POLR2H	20	PTX3	Down	GATAD2A	29	FGG
Up	FOXJ2	20	TIPARP	Down	ZNF366	29	GPX8
Up	ZNF263	19	IRS1	Down	ARNT	29	CD2
Up	SMC3	19	RND3	Down	ZNF175	29	CCNB1
Up	GATAD2A	19	GTPBP4	Down	BCOR	29	BBC3
Up	PBX2	19	CYP11A1	Down	SIRT6	28	DDR1
Up	HMG20A	19	FOSL2	Down	SMARCA4	28	KIF22
Up	PRDM10	19	CYP17A1	Down	TEAD3	28	UBD
Up	JUND	19	PTP4A1	Down	ARID1B	28	PBK
Up	EED	19	PDGFRA	Down	GATA2	28	POPDC2
Up	ZNF335	18	AASS	Down	TFAP4	28	IDH2
Up	ZNF366	18	FUBP1	Down	NFIA	28	HIST1H2BO
Up	GFI1B	18	CNN3	Down	SP2	27	HIST1H2BL
Up	SMARCA4	18	KCTD14	Down	DRAP1	27	MMP9
Up	SIRT6	18	EGR1	Down	SMARCE1	27	PMAIP1
Up	ZKSCAN1	18	C14orf132	Down	ZNF639	27	BUB1
Up	KLF6	18	GSTA4	Down	GLI4	27	ZBED3
Up	ID3	18	CYB561	Down	ZNF83	27	FUK
Up	GLIS1	18	CRLF1	Down	ZNF18	26	CCNG2
Up	MTA2	18	SAA1	Down	SOX5	26	EXO1
Up	RNF2	17	ADM	Down	ATF3	26	UGT1A6
Up	SUPT5H	17	SDF2L1	Down	ZNF584	26	CXCL9
Up	ZBTB40	17	MSI2	Down	ZHX2	26	MC1R
Up	NR2F2	17	RAMP1	Down	TBX21	26	GALNT10

Table 8 (continued)

Regulation	TF	Degree	Target gene	Regulation	TF	Degree	Target gene
Up	THAP1	17	IER3	Down	PML	26	MSH2
Up	ZNF384	17	PTP4A1	Down	ZNF335	25	HIST1H2BN
Up	SP7	17	ID2	Down	GTF2A2	25	CD69
Up	MTA1	17	HES1	Down	THRAP3	25	OIP5
Up	NCOA1	17	CEBPD	Down	JUNB	25	KIAA0922
Up	PRDM1	17	HOXA7	Down	CTCF	24	MMP9
Up	TEAD1	17	HSPA5	Down	RARA	24	ZNF266
Up	KLF4	16	DLL1	Down	HDAC1	24	CCNB2
Up	ETV1	16	SNAI1	Down	EZH2	24	GPR150
Up	LEF1	16	RAB34	Down	TRIM22	24	NR3C1
Up	ADNP	16	RAB21	Down	SMAD4	24	FBXO32
Up	ZNF175	16	ECHDC3	Down	YY1	23	UGT1A6
Up	ATF4	16	XBP1	Down	DPF2	23	DNMT3B
Up	ZNF639	16	CTSD	Down	ZNF558	23	RAI14
Up	HCFC1	16	JUNB	Down	CREB3	23	HMBOX1
Up	BACH1	16	IL6	Down	HCFC1	23	RANBP17
Up	MIXL1	16	GABARAPL1	Down	TEAD1	22	FN1
Up	MEF2D	16	CXCL2	Down	TSHZ1	22	PBK
Up	GTF2A2	16	KCNK5	Down	USF2	22	NR3C1
Up	ZNF83	16	TIPARP	Down	SP7	22	CHAF1A
Up	CCNT2	16	TLX2	Down	TRIM24	22	POLD1
Up	HMBOX1	16	HBB	Down	TBP	22	KIAA0101
Up	GLI4	15	CRLF1	Down	KLF4	21	CDT1
Up	MAX	15	MRAS	Down	MTA2	21	IGJ
Up	KLF13	15	SDF2L1	Down	ZNF121	21	DEF6
Up	TRIM22	15	TRIM22	Down	ZNF341	21	MYBL2
Up	RELA	15	C1S	Down	RAD21	21	HOMER1
Up	DDX20	15	ZBED1	Down	SIN3B	21	NUDT1
Up	USF2	15	NR4A3	Down	ZNF384	21	ENC1
Up	EGR2	14	ABR	Down	HES1	21	F11R
Up	ZNF623	14	WFDC1	Down	EED	20	MICB
Up	TSHZ1	14	TGFBR3	Down	ZNF263	20	GRIN2C
Up	SIN3B	14	AOC3	Down	FOXA3	20	PLK2
Up	HDAC1	14	YWHAZ	Down	GMEB2	20	CDCA7
Up	TBX21	14	SELK	Down	STAT1	20	MCM2
Up	CBFB	14	DNAJB9	Down	TRIM28	20	LAMB1
Up	RFX1	14	SYT13	Down	ZNF382	19	BRD8
Up	TCF7	14	TNFRSF11B	Down	RNF2	19	ANXA4
Up	ZNF584	14	UNC5B	Down	IRF2	19	ANLN
Up	CUX1	14	PRKAR1A	Down	ZNF207	19	MAPKAPK5
Up	ZNF18	14	FOXK2	Down	TARDBP	19	ZG16B
Up	HHEX	13	AQP11	Down	ATF4	18	HIST1H2BE
Up	TRIM24	13	SOAT1	Down	KAT2A	18	FANK1
Up	MITF	13	GK	Down	EGR2	17	EML1
Up	NFE2L2	12	NDRG1	Down	PRDM10	17	LRIG3
Up	ZNF558	12	NOLC1	Down	ZNF512	17	CYP3A5
Up	PKNOX1	12	S100A8	Down	CDC5L	17	KCNK1
Up	ZNF121	12	ATP5L	Down	MXI1	17	BIRC5
Up	CREB3	12	HSPA1A	Down	POU2F2	17	PMAIP1
Up	ARID1B	12	DUSP5	Down	HDAC6	16	ADA
Up	IKZF1	12	SEMA3B	Down	HDAC2	16	SLC2A4RG

Table 8 (continued)

Regulation	TF	Degree	Target gene	Regulation	TF	Degree	Target gene
Up	ZNF512	11	ATP1B3	Down	THAP1	16	CDKN3
Up	ZNF7	11	DDC	Down	NR2F2	16	COL1A1
Up	GMEB2	11	SELK	Down	MBD4	16	TP53INP1
Up	ZNF143	11	DNAJB9	Down	HNF4G	16	COL27A1
Up	RAD51	10	ADRA2C	Down	PRDM1	16	HOXA13
Up	HDAC6	10	ANGPTL4	Down	ZNF623	16	ZNF404
Up	ZBTB1	10	AKR1B1	Down	GFI1B	16	PRSS16
Up	HDAC2	10	IL1R2	Down	TCF7	16	HIST1H4H
Up	ZBTB17	10	HOXA9	Down	GTF2B	16	CDCA5
Up	RFX3	10	ALDH3A2	Down	NFYB	16	FANCG
Up	CTBP1	10	HOXB2	Down	CUX1	16	MMP9
Up	CDC5L	10	CEBPB	Down	EBF1	15	KLK1
Up	ZNF382	10	THBS1	Down	RELA	15	HIST1H2BE
Up	SCRT1	10	GSTT2	Down	PBX2	15	HIST1H2BC
Up	GATA3	10	HSPA5	Down	GLIS1	15	TIGD7
Up	EBF1	9	CD38	Down	NFIC	15	PMAIP1
Up	KDM5A	9	SDF2L1	Down	ZNF143	14	AHR
Up	NFE2	9	JUNB	Down	MTA1	14	LCN2
Up	ARNT	9	LDLR	Down	CTBP2	14	ST6GALNAC2
Up	RCOR1	9	AQP11	Down	ZNF407	14	GALNT10
Up	EP300	9	PI16	Down	CEBPA	14	DEPDC7
Up	TARDBP	9	GSTA4	Down	SUZ12	14	HHEX
Up	RUNX1	9	GNAZ	Down	NFE2	14	RFC5
Up	TAL1	9	G0S2	Down	NFATC1	14	HIST1H2BB
Up	ZNF207	9	TIPARP	Down	MTA3	14	HIST1H4K
Up	HDAC8	8	SNAI1	Down	TAL1	13	MUC20
Up	THRAP3	8	HBB	Down	GATA1	13	IQSEC1
Up	STAT1	8	IKBKAP	Down	CEBPD	13	CLDN1
Up	GTF2B	8	IER3	Down	FOXA2	13	HIST1H2BD
Up	MNT	7	VASN	Down	TEAD4	13	SUCNR1
Up	PML	7	RAB34	Down	BHLHE40	13	DMTF1
Up	CEBPA	7	HSPA4L	Down	GATA3	12	MAGED2
Up	IRF2	7	SDF2L1	Down	FOSL2	12	CAP2
Up	SREBF2	6	AKR1B1	Down	RFX1	12	DDR1
Up	GATAD2B	6	EGR1	Down	ZNF146	12	HIST1H4K
Up	ZNF407	6	CLDN5	Down	MYC	12	MTL5
Up	TBP	6	MT1X	Down	CEBPB	12	HLA-DQB1
Up	MYC	6	NR4A3	Down	RFX3	12	DYRK2
Up	NFATC1	6	NDRG1	Down	SREBF2	12	PRC1
Up	GATA1	6	CYB561	Down	FOXK2	11	ZNF302
Up	MTA3	6	JUNB	Down	MAX	11	CCNB1
Up	CBX8	6	RPRM	Down	ZNF7	11	GADD45A
Up	PTTG1	6	IL6	Down	CHD7	11	HIST1H2BO
Up	PRDM2	5	NPC1	Down	SCRT2	10	FHOD1
Up	ZNF146	5	PEG10	Down	RCOR1	10	PRSS16
Up	SIX4	5	SNAI1	Down	ZNF202	10	PPP1R13L
Up	ATF2	5	PLAT	Down	ATF2	10	IGJ
Up	EHMT2	5	CRH	Down	IRF3	10	HIST1H2BB
Up	FOXA2	5	PTGIR	Down	ZBTB1	9	XRCC1
Up	TEAD4	5	FOXK2	Down	JUND	9	PSAT1
Up	DEK	5	ECE2	Down	MAFF	9	OIP5

Table 8 (continued)

Regulation	TF	Degree	Target gene	Regulation	TF	Degree	Target gene
Up	ZNF202	5	PGM3	Down	EP300	9	PBK
Up	ZNF217	5	MGST1	Down	E2F6	9	RRM2
Up	MAFK	5	GNAZ	Down	ZNF547	8	FER1L4
Up	PTRF	5	PRKAR2B	Down	MITF	8	HIST1H2BI
Up	TEAD2	5	RARRES2	Down	SCRT1	8	NEK3
Up	CHD4	4	CREM	Down	ZNF217	8	HSPB1
Up	RXRA	4	APOC1	Down	DIDO1	8	NUDT1
Up	MXI1	4	STAT3	Down	RUNX1	8	PTCD1
Up	ZNF488	4	SOAT1	Down	JUN	7	HIST1H2BN
Up	MYB	4	MAT2A	Down	PYGO2	7	HIST1H2BE
Up	DIDO1	4	CXCL2	Down	MAFK	7	ZWINT
Up	ZNF16	4	HOXA5	Down	MYB	7	KIF22
Up	DNMT1	4	SFPQ	Down	TAF1	6	HIST1H2BF
Up	ZHX1	4	JUNB	Down	CTBP1	6	LRIG3
Up	SREBF1	4	LDLR	Down	ZNF239	6	RNFT2
Up	POU5F1	3	FBLN1	Down	DEK	6	BMF
Up	SCRT2	3	ADAMTS1	Down	ZBTB17	6	HOMER1
Up	ZNF264	3	DNAJB9	Down	NFYA	6	CDCA8
Up	JUN	3	CEBPB	Down	SMC3	6	WNT5A
Up	FOS	3	G0S2	Down	NFE2L2	6	GADD45A
Up	SPI1	3	NEDD9	Down	ZHX1	5	ASPM
Up	RUNX3	3	DUSP5	Down	ZNF641	5	DAND5
Up	ZNF547	3	KCNK5	Down	HLF	5	SERPINA3
Up	E2F6	3	FOXK2	Down	SETDB1	5	ZNF404
Up	PYGO2	3	HSPA1A	Down	NFE2L1	5	HIST1H1C
Up	ETV6	3	GNAZ	Down	MNT	4	APOBEC3A
Up	TCF7L2	3	SDF2L1	Down	ZNF16	4	ROR1
Up	ZNF641	3	GSTA4	Down	POU5F1	4	DNMT3B
Up	CHD7	3	PDGFRA	Down	ZNF274	4	ZNF443
Up	POU2F2	3	TIPARP	Down	TBX3	4	PLA2G1B
Up	NONO	3	SOAT1	Down	RBBP5	4	TIMELESS
Up	ZC3H11A	2	ADM	Down	STAT3	4	MCM8
Up	UBTF	2	GSTA4	Down	PKNOX1	4	HIST1H2BF
Up	ZNF239	2	SLC27A6	Down	ZNF488	3	ITPKA
Up	NFIC	2	CD83	Down	ZNF585B	3	FBXO32
Up	TSC22D4	2	TSC22D4	Down	RUNX3	3	GPR150
Up	MCM3	2	CLDN5	Down	SPI1	3	IER5
Up	SRF	2	EGR1	Down	FOS	3	BTBD11
Up	ELK4	2	JUNB	Down	MAFG	3	HIST1H2BL
Up	POLR3A	2	GABARAPL1	Down	UBTF	3	DDB2
Up	YBX1	2	GNAZ	Down	ZC3H11A	3	C14orf80
Up	SETDB1	2	GTPBP4	Down	GATAD2B	3	KIF22
Up	ETS2	2	HSPA1A	Down	PRDM2	3	CCNE1
Up	MAFF	2	PLA2G4A	Down	BCLAF1	3	HIST1H2BJ
Up	HLF	2	IGFBP6	Down	BDP1	3	PRSS16
Up	KAT2A	2	NR4A1	Down	GTF3C2	3	HIST1H2BI
Up	ZFP41	1	ADAMTS1	Down	BRF1	3	HIST1H4H
Up	MCM5	1	GNAZ	Down	POLR3A	3	PRSS16
Up	FOXA1	1	GNAZ	Down	ETV6	3	STK36
Up	MCM7	1	GNAZ	Down	TEAD2	3	RHOBTB3
Up	CEBPZ	1	GNAZ	Down	ZNF140	3	ZNF700

Table 8 (continued)

Regulation	TF	Degree	Target gene	Regulation	TF	Degree	Target gene
Up	ZNF138	1	HOXA5	Down	ZFP41	2	BBC3
Up	PRDM12	1	HOXA9	Down	ZNF8	2	POLD1
Up	PPARGC1A	1	HSPA1A	Down	SIX4	2	MUC20
Up	HSF1	1	HSPA1A	Down	SIX5	2	ZNF133
Up	USF1	1	ID2	Down	TCF7L2	2	HIST1H2BD
Up	HNF4A	1	IGFBP6	Down	BATF	2	FANK1
Up	ZNF8	1	JUNB	Down	RXRA	2	FGG
Up	BCL3	1	NOLC1	Down	ZNF264	2	GMNN
Up	ZZZ3	1	NR2F1	Down	SREBF1	2	MAPKAPK5
Up	E2F4	1	PDE8A	Down	STAT5A	2	HIST1H2BB
Up	AEBP2	1	PEG10	Down	TCF3	2	HIST1H1C
Up	NANOG	1	PLEK2	Down	CEBPZ	2	KIAA0101
Up	NR3C1	1	PNMT	Down	TSC22D4	2	TMEM191A
Up	MAFG	1	PRKAR2B	Down	RFX5	2	TP53INP1
Up	CHD2	1	RAB34	Down	CHD4	2	KIF11
Up	ZMIZ1	1	SDF2L1	Down	HNF4A	2	SLC2A4RG
Up	SMAD2	1	SDF2L1	Down	ETS2	1	BBC3
Up	ZNF585B	1	TLX2	Down	BCL3	1	BBC3
				Down	MCM7	1	BBC3
				Down	CHD2	1	CDCA2
				Down	USF1	1	COL1A1
				Down	ZNF354C	1	FABP3
				Down	FOXA1	1	FANK1
				Down	TBL1XR1	1	GADD45A
				Down	PRDM12	1	HOXA13
				Down	PPARGC1A	1	HSPB1
				Down	HSF1	1	HSPB1
				Down	YBX1	1	LY6D
				Down	NONO	1	LY6D
				Down	EHMT2	1	NPTX2
				Down	CBX8	1	PRSS16
				Down	HDAC8	1	PSAT1
				Down	ZNF138	1	ZNF302

Degree—no of target gene interact with TF. We taken any one target gene in table

TF transcription factors

[137], COL3A1 [138], LAMA3 [139], and LAMB1 [140] were linked with invasion of different cancer cells such as gastric cancer, bladder cancer, head and neck cancers, and colorectal cancer, but these genes may be diagnosed with growth of ACC. Mutation in genes such as EXO1 [141] and POLD1 [142] were associated with pathogenesis of colorectal cancer, but alteration in this gene may be identified with growth of ACC. SNP in LIG1 was involved in progression of lung cancer [143], but this gene may be responsible for development of ACC. HIST1H2BB, HIST1H2BC, HIST1H2BD, HIST1H2BE, HIST1H2BF, HIST1H2BH, HIST1H2BI, HIST1H2BJ, HIST1H2BL, HIST1H2BN, HIST1H2BO, HIST1H4F, HIST1H4H, HIST1H4J, HIST1H4K, HLA-DRB4, MAT1A, COL14A1, COL27A1, COL4A5, COL5A2, RFC4, and RFC5 were novel biomarkers for pathogenesis of ACC in these pathways.

In GO enrichment analysis, up regulated genes were mainly associated with all GO categories (BP, CC and MF) such as blood vessel morphogenesis, extracellular matrix, and heparin binding. Genes such as adrenomedullin (ADM) [144], apolipoprotein E (APOE) [145], GATA6 [146], and RARRES2 [147] were responsible for pathogenesis of ACC. Genes such as CDH2 [148], CITED1 [149], FZD4 [150], STARD13 [151], XBP1 [152], and latexin (LXN) [153] were associated with invasion of different cancer cells such as lung cancer, colorectal cancer, prostate cancer, breast cancer, and thyroid cancer, but these genes may be liable for invasion of ACC cells. Methylation inactivation of tumor

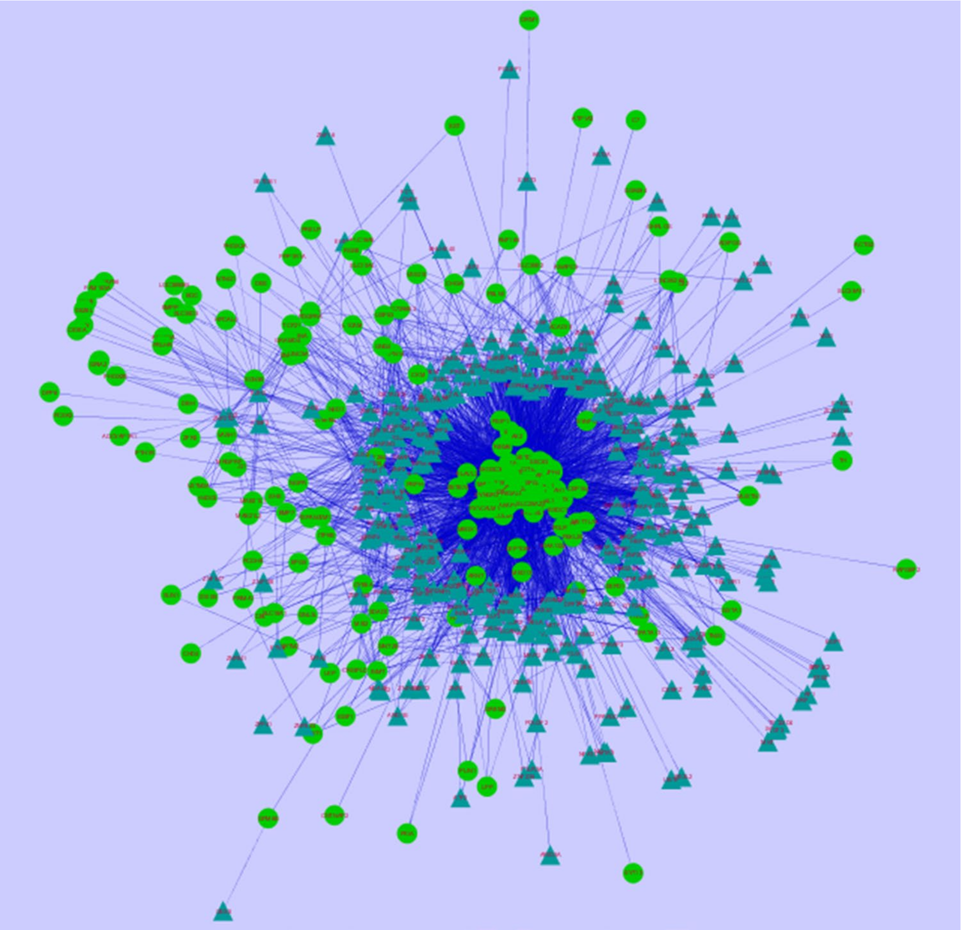


Fig. 14 TF–gene network of predicted target up regulated genes. Pink triangles are TFs and green circles are target upregulated genes. Yellow lines means interaction with adjutant genes or TFs

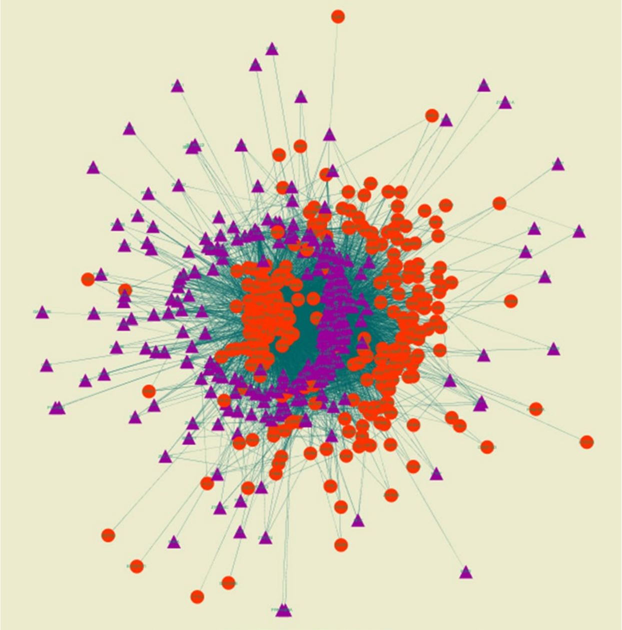


Fig. 15 TF–gene network of predicted target down-regulated genes. Blue triangles are TFs and pink circles are target down-regulated genes. Yellow lines means interaction with adjutant genes or TFs

suppressor genes such as DLL1 [154], HAND2 [155], and UNC5B [156] were identified with progression of different cancer such as lung cancer endometrial cancer and colorectal cancer, but loss of these genes may be involved in development of ACC. High expression of genes such as ENPP2 [157], GJA1 [158], HES1 [159], RAMP1 [160], SIRT1 [161], TFAP2B [162], TNFRSF11B [163], and SAA1 [164] were important for advancement of different cancer such as hepatocellular carcinoma, endometrial cancer, colon cancer, prostate cancer, lung cancer, and gastric cancer, but elevated expression of these genes may be diagnosed with ACC. Genes such as HOXA5 [165] and HOXA7 [166] were linked with cell cycle progression in different cancer such as breast cancer and ovarian cancer, but these genes may be involved in cell cycle progression in ACC. SNP in NRXN3 was important for development of breast cancer [167], but this polymorphic gene may be involved in development of ACC. Low expression of TGFBR3 was responsible for advancement of prostate cancer [168], but loss of this gene may associated with growth of ACC. Platelet-derived growth factor receptor, alpha polypeptide (PDGFRA), SCG2, TCDD-inducible poly(ADP-ribose) polymerase (TIPARP),

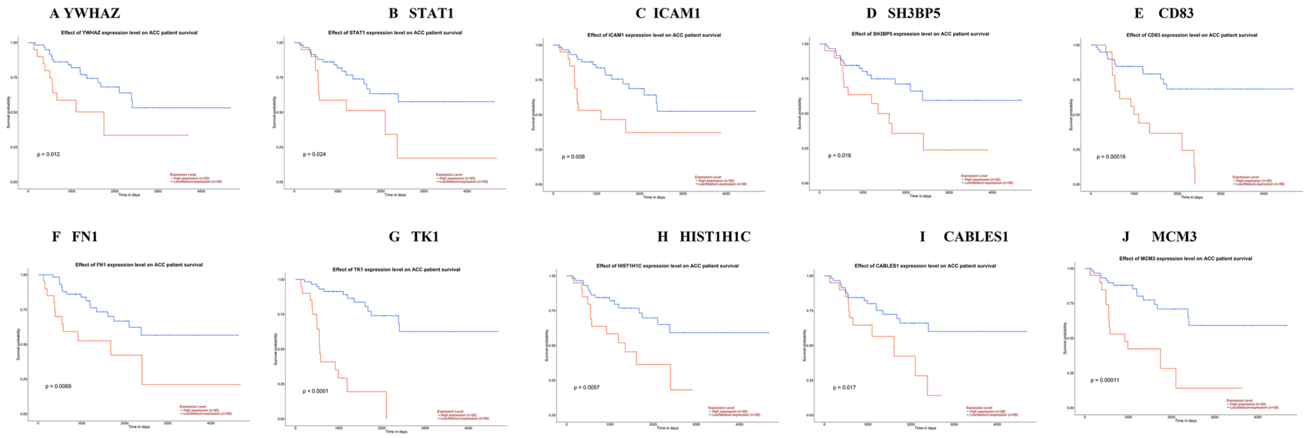


Fig. 16 Kaplan–Meier survival curves using TCGA data validate the prognostic value of genes expressed in ACC. (Blue is low expression and Red is high expression)

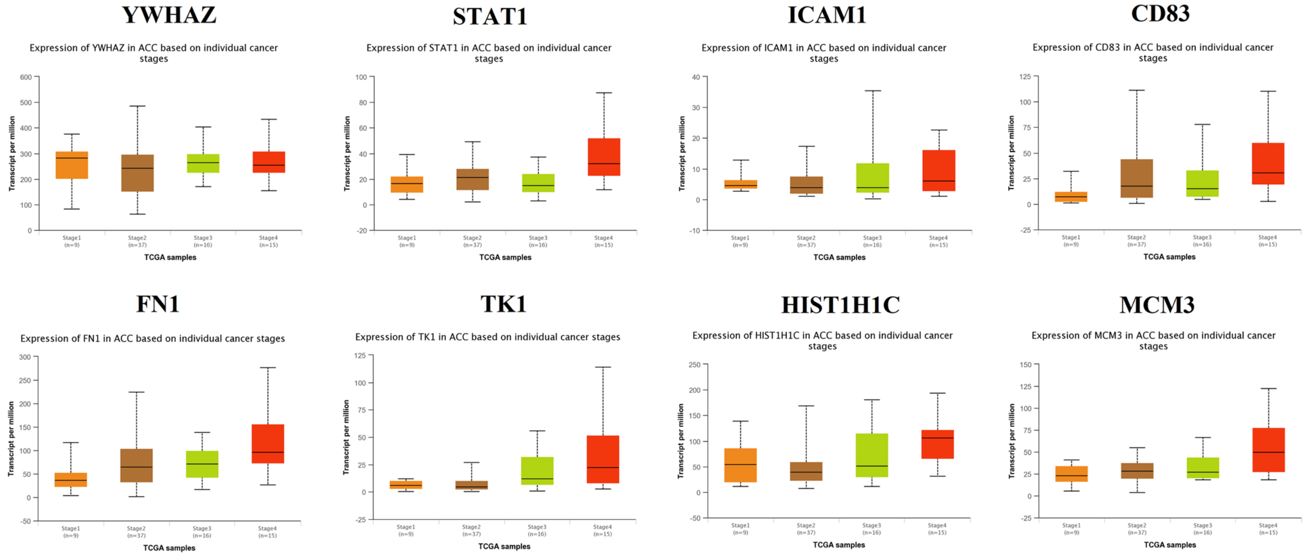


Fig. 17 Validation of the expression of hub genes in the TCGA database. High expression of hub genes in stages 4. ACC:Adrenocortical carcinoma

and IL1RL1 were novel biomarkers for pathogenesis of ACC in these GO categories. Meanwhile, down regulated genes were mainly associated with all GO categories such as cell cycle phase transition, chromosome, centromeric region, and protein dimerization activity. High expression of genes such as anillin, actin binding protein (ANLN) [169], NEK2 [170], timeless homolog (TIMELESS) [171], TPX2 [172], TTK protein kinase (TTK) [173], CDCA8 [174], KIF18A [175], OIP5 [176], SPC25 [177], ZWINT [178], asparagine synthetase (ASNS) [179], E2F8 [180], LCN2 [181], and RAB11FIP4 [182] were important for progression of different cancers such as pancreatic cancer, breast cancer, lung cancer, colorectal cancer, gastric cancer, ovarian cancer, and hepatocellular carcinoma, but increased expression of these genes may be associated with development of ACC. Genes such as BIRC5 [183], BUB1 [184], CCNB1 [185], CCNB2 [186], CDCA5 [187], CDKN3 [188], centromere protein F (CENPF) [189], and SPAG5 [190] were associated with proliferation of different cancer cells such as breast cancer, gastric cancer, hepatocellular carcinoma, and ovarian cancer, but these genes may be linked with proliferation of ACC cells. Methylation inactivation of tumor suppressor genes such as CABLES1 [191], GADD45A [192], PLK2 [193], and NR3C1 [194] were involved in pathogenesis of different cancers such as ovarian cancer, breast cancer, and colorectal cancer, but loss these genes may be identified with development of ACC. SNP in genes such as hyaluronan-mediated motility receptor (HMMR) [195]. DNMT3B [196], aryl

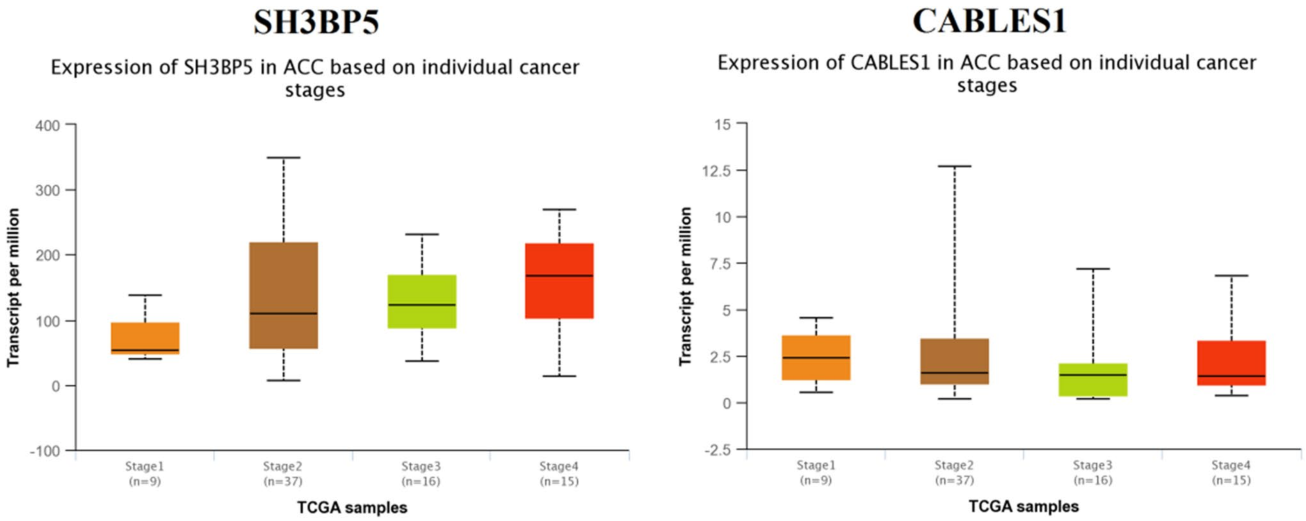


Fig. 18 Validation of the expression of hub genes in the TCGA database. High expression of hub genes in stages 2 and 1. ACC:Adrenocortical carcinoma

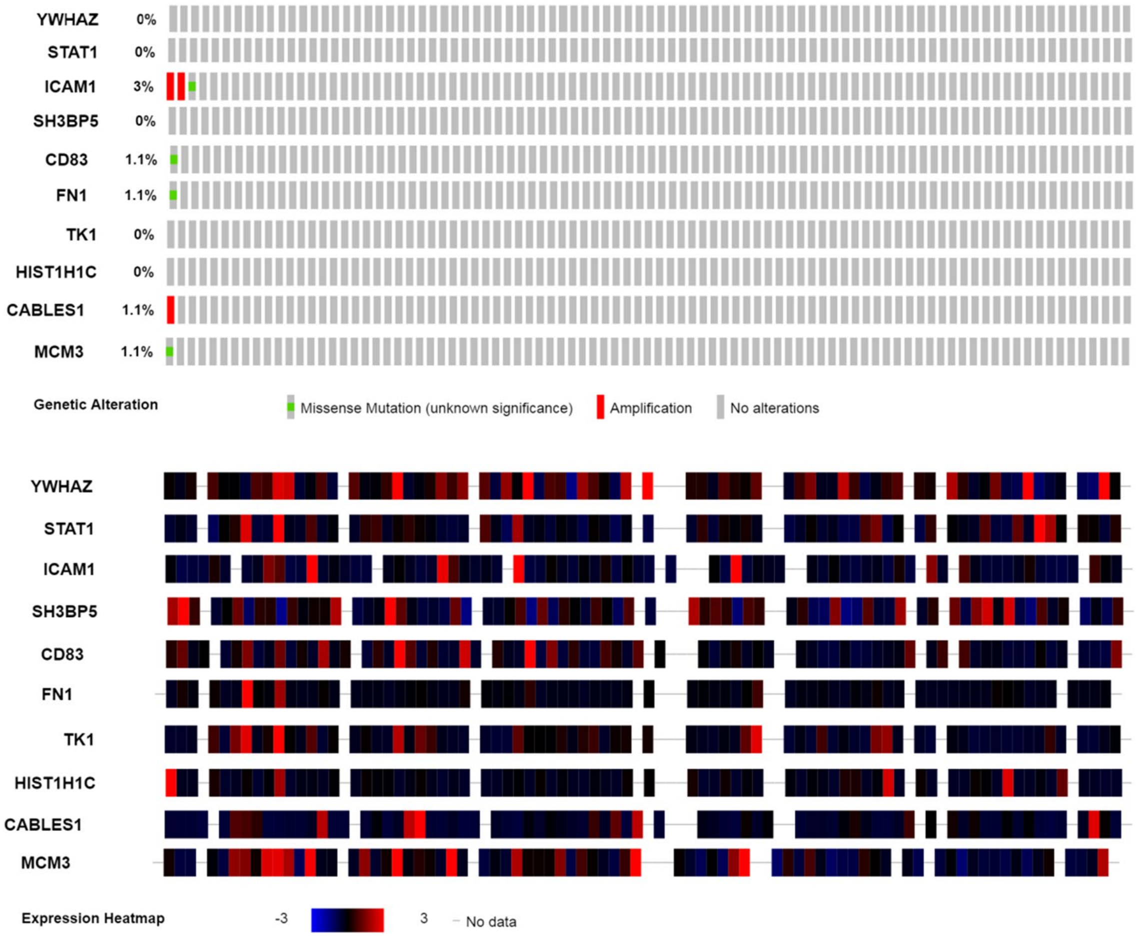


Fig. 19 Genetical alteration analysis (genetical alterations towards these ten genes)

hydrocarbon receptor (AHR) [197] hydroxyprostaglandin dehydrogenase 15-(NAD) (HPGD) [198], and UGT1A6 [199] were liable for advancement of different cancer such as breast cancer, lung cancer, and colorectal cancer, but these polymorphic genes may be linked with development of ACC. Alteration in genes such as MAD2L1 [200] and BARD1 [201] were associated with pathogenesis of breast cancer, but mutation in this gene may be involved in development of ACC. Genes such as maternal embryonic leucine zipper kinase (MELK) [202], RRM2 [203], NR0B1 [204], and TOP2A [14] were important for pathogenesis of ACC. Alteration in tumor suppressor gene PLAGL1 was liable for growth of pheochromocytomas [205], but mutation in this gene may be associated with pathogenesis of ACC. CEP192, KNTC1, MCM8, KIF22, NUP107, STAG3, BTBD11, CD2, CD3D, DPP4, fibroblast activation protein, alpha (FAP) granzyme A (granzyme 1, cytotoxic T-lymphocyte-associated serine esterase 3) (GZMA), H2BFS, hematopoietically expressed homeobox (HHEX), HOMER1, v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog (KIT), NCOA6, SRGAP2, and TCFL5 were novel biomarkers for pathogenesis of ACC in these GO categories.

In this study, we finally identify five hub genes (up regulated) were in PPI network with high node degree such as YWHAZ, HSPA5, STAT3, APOE, and GRK5. High expression of tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide (YWHAZ) was responsible for progression of head and neck cancer [206], but elevated expression of this gene may be identified with growth of ACC. Genes such as HSPA5 [207] and GRK5 [208] were associated with invasion of different cancer cells such as colorectal cancer and prostate cancer, but these genes may be liable for invasion of ACC cells. Five hub genes (up regulated) were in PPI network with high betweenness such as YWHAZ, HSPA5, STAT3, TH, and CD83. SNP in CD83 was diagnosed with growth of cervical cancer [209], but this polymorphic gene may be involved in development of ACC. Five hub genes (up regulated) were in PPI network with high stress such as YWHAZ, HSPA5, ICAM1, HOXB2, and STAT3. ICAM1 was linked with invasion of breast cancer cells [210], but this gene may be associated with invasion of ACC cells. High expression of HOXB2 was involved in pathogenesis of cervical cancer [211], but elevated expression of this gene may be responsible for progression of ACC. Five hub genes (up regulated) were in PPI network with high closeness such as YWHAZ, HSPA5, NR4A1, IRS1, and MAP3K5. MAP3K5 was important for invasion of prostate cancer cells [212], but this gene may be linked with invasion of ACC cells. Five hub genes (up regulated) were in PPI network with low clustering coefficient such as CRLF1, CRH, ARHGAP18, FJX1, and FMO3. Corticotropin releasing hormone (CRH) was liable for progression of pheochromocytomas [213], but this gene may be associated with advancement of ACC. ARHGAP18 was identified with invasion of breast cancer cells [214], but this gene may be involved in invasion of ACC cells. High expression of FJX1 was diagnosed with growth of nasopharyngeal carcinoma [215], but over expression of this gene may be identified with progression of ACC. SNP in FMO3 was responsible for advancement of colorectal cancer [216], but this polymorphic gene may be associated with development of ACC. Meanwhile, five hub genes (down regulated) were in PPI network with high node degree such as FN1, VCAM1, UBD, BARD1, and TK1. High expression of genes such as VCAM1 [217] and ubiquitin D (UBD) [218] were responsible for pathogenesis of different cancers such as gastric cancer and colon cancer, but elevated expression of these genes may be liable for growth of ACC. Five hub genes (down regulated) were in PPI network with high betweenness such as FN1, UBD, VCAM1, BARD1, and TK1. Five hub genes (down regulated) were in PPI network with high stress such as FN1, UBD, VCAM1, SLPI, and BARD1. Secretary leukocyte protease inhibitor (SLPI) was linked with invasion of ovarian cancer cells [219], but this gene may be involved in invasion of ACC cells. Five hub genes (down regulated) were in PPI network with high closeness such as FN1, VCAM1, MCM3, PHGDH, and MCM6. High expression phosphoglycerate dehydrogenase (PHGDH) was responsible for pathogenesis of melanoma [220], but over expression of this gene may be identified with growth of ACC. Five hub genes (down regulated) were in PPI network with low clustering coefficient such as CYP3A5, POPDC2, PNLIPRP2, KIAA1407, and CX3CR1. SNP in CYP3A5 was important for pathogenesis of breast cancer [221], but this polymorphic gene may associated with development of ACC. CX3CR1 was linked with invasion of prostate cancer cells [222], but this gene may be involved in invasion of ACC cells. POPDC2, PNLIPRP2, and KIAA1407 were novel biomarkers for pathogenesis of ACC in these PPI network.

Hub genes (up regulated) such as YWHAZ, GRK5, NOLC1, ID2, STAT3, HES1, NR4A1, ZNF331, APOE, PLAT, C1S, SERPING1, HP, APOC1, SH3BP5, STAT1, IPO7, and HSPA4L were in all four modules. NOLC1 was associated with proliferation of hepatocellular carcinoma cell [223], but this gene may be responsible for progression of ACC cells. High expression of genes such as ID2 [224], APOC1 [225], and HSPA4L [226] were involved in pathogenesis of different cancer such as pancreatic cancer, lung cancer, and hepatocellular carcinoma, but increase expression these genes may be linked with growth of ACC. Methylation inactivation of tumor suppressor gene ZNF331 was important for development of colorectal cancer [227], but loss of this gene may be liable for growth of ACC. SNP in haptoglobin (HP) was associated with pathogenesis of breast cancer [228], but this polymorphic gene may be liable for growth of ACC. IPO7 was involved in proliferation of prostate cancer cells [229], but this gene may be associated with proliferation of ACC cells. C1S and SH3BP5 were novel biomarkers for pathogenesis of ACC in these modules. Meanwhile, hub genes (down regulated) such as VCAM1, FN1, MCM3, MCM2, MCM6, UBD, MAGED2, HIST1H1C, MAD2L1, PHGDH, HSPB1, HIST1H2BJ, UHRF1, NCOR2, TOP2A, PBK, ASNS, TMPO, HMGB2, HIST1H2BL, TYMS, CHAF1B, CCNE1, POLD1, CDT1, and PRC1 were in all four modules. Methylation inactivation of tumor suppressor gene HSPB1 was responsible for progression of prostate cancer [230], but loss of this gene may be identified with pathogenesis of ACC. High expression of genes such as UHRF1 [231] and PDZ binding kinase (PBK) [232] were important for advancement of different cancer such as lung cancer and prostate cancer, but elevated expression of these genes may be associated with development of ACC. NCOR2 was responsible for proliferation of glioblastoma cells [233], but this gene may be linked with proliferation of ACC cells. MAGED2 HIST1H1C, thymopoietin (TMPO), CHAF1B, and PRC1 were novel biomarkers for pathogenesis of ACC in these modules.

Target genes (up regulated) such as YWHAZ, GATA6, LDLR, BZW1, and IGFBP5 were in target genes–miRNA regulatory network. BZW1 was novel biomarker for pathogenesis of ACC in this network. Meanwhile, target genes (down regulated) such as TXNIP, MAPKAPK5, PMAIP1, RAD51, and MICA were in target genes–miRNA regulatory network. Decrease expression of tumor suppressor genes such as thioredoxin interacting protein (TXNIP) [234] and PMAIP1 [235] was diagnosed with growth of different cancer types such as thyroid cancer and pancreatic cancer, but loss of expression of these genes may liable for pathogenesis of ACC. High expression of RAD51 was involved in pathogenesis of breast cancer [236], but elevated expression of this gene may be linked with growth of ACC. MAPKAPK5 and MHC class I polypeptide-related sequence A (MICA) were novel biomarkers for pathogenesis of ACC in this network.

Target genes (up regulated) such as HSPA1A, PHOX2B, H19, CEBPD, and DNAJC3 were in target genes–TF regulatory network. HSPA1A was associated with pathogenesis of colorectal cancer [237], but this gene may be important for development of ACC. Inactivation of H19 was involved in pathogenesis of ACC [238]. PHOX2B and DNAJC3 were novel biomarkers for pathogenesis of ACC in this network. Meanwhile, target genes (down regulated) such as F11R, CHAF1B, FANCG, CENPF, and XRCC1 were in target genes–TF regulatory network. F11R was linked with advancement of glioma [239], but this gene may be associated with development of ACC. SNP in genes such as fanconianemia, complementation group G (FANCG) [240], and XRCC1 [241] were liable for progression of different cancers such as pancreatic cancer and breast cancer, but these genes may be liable for growth of ACC.

Survival analysis revealed that genes such as YWHAZ, STAT1, ICAM1, SH3BP5, CD83, FN1, TK1, HIST1H1C, CABLES1, and MCM3 were predicting shorter survival of ACC. Expression levels revealed that hub genes such as STAT1, ICAM1, CD83, FN1, TK1, HIST1H1C, and MCM3 were highly expressed in ACC (stages 4), meanwhile those such as SH3BP5 and CABLES1 were highly expressed in ACC (stage 2 and stage 1).

In conclusion, we diagnosed several hub genes and pathways that were closely related to the initiation and progression of ACC using a series of bioinformatics analyses of DEGs in cancer and normal samples. Identification of the associated genes, YWHAZ, FN1, GRK5, VCAM1, GATA6, TXNIP, HSPA1A, and F11R, provided greater insight into the specific molecular mechanisms underlying ACC occurrence and development, especially in terms of the pathways involved in catecholamine biosynthesis, aldosterone synthesis and secretion, pyrimidine deoxyribonucleosides salvage, and systemic lupus erythematosus. Upon further experimental validation of these results, these genes may serve as potential research targets for therapy and thereby contribute to greater understanding of the molecular mechanisms underlying the progression of ACC.

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Author contributions Ali Mohamed Alshabi associated with project administration, methodology, and review and editing; Ali Mohamed Alshabi, Ibrahim Ahmed Shaikh, and Basavaraj Vastrad participated in writing original draft and investigation; and Chanabasayya Vastrad performed software, supervision, formal analysis, and validation. Basavaraj Vastrad and Ali Mohamed Alshabi made substantial contributions to acquisition of resources, formal analysis, and validation.

Availability of data and materials The datasets supporting the conclusions of this article are available in the GEO (Gene Expression Omnibus) (https://www.ncbi.nlm.nih.gov/geo/) repository. [(GSE19775) (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc= GSE19775)].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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

Informed consent No informed consent because this study does not contain any human or animal participants.

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