

Received: 2016.03.01
Accepted: 2016.04.22
Published: 2017.01.12

Identification of Key Transcription Factors Associated with Lung Squamous Cell Carcinoma

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Source of support: Departmental sources

Background: Lung squamous cell carcinoma (lung SCC) is a common type of lung cancer, but its mechanism of pathogenesis is unclear. The aim of this study was to identify key transcription factors in lung SCC and elucidate its mechanism.





Material/Methods: Six published microarray datasets of lung SCC were downloaded from Gene Expression Omnibus (GEO) for integrated bioinformatics analysis. Significance analysis of microarrays was used to identify differentially expressed genes (DEGs) between lung SCC and normal controls. The biological functions and signaling pathways of DEGs were mapped in the Gene Ontology and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway database, respectively. A transcription factor gene regulatory network was used to obtain insights into the functions of DEGs.

Results: A total of 1,011 genes, including 539 upregulated genes and 462 downregulated genes, were filtered as DEGs between lung SCC and normal controls. DEGs were significantly enriched in cell cycle, DNA replication, p53 signaling pathway, pathways in cancer, adherens junction, and cell adhesion molecules signaling pathways. There were 57 transcription factors identified, which were used to construct a regulatory network. The network consisted of 736 interactions between 49 transcription factors and 486 DEGs. NFIC, BRCA1, and NFATC2 were the top 3 transcription factors that had the highest connectivity with DEGs and that regulated 83, 82, and 75 DEGs in the network, respectively.

Conclusions: NFIC, BRCA1, and NFATC2 might be the key transcription factors in the development of lung SCC by regulating the genes involved in cell cycle and DNA replication pathways.

MeSH Keywords: **Activating Transcription Factors • Carcinoma, Squamous Cell • Gene Expression Profiling • Gene Regulatory Networks • Lung Neoplasms**

Full-text PDF: <http://www.medscimonit.com/abstract/index/idArt/898297>

 2255  6  2  38



Background

Lung cancer is the most frequent cause of cancer death and an estimated 1.8 million new cases occurred in 2012 worldwide, accounting for about 13% of total cancer diagnosis [1]. Lung cancer is the leading cancer site in males, including 17% of the total new cancer cases and 23% of the total cancer deaths in 2008 worldwide [2]. Tobacco use is the major risk factor for lung cancer [3].

Lung cancer is classified as non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) according to histopathology appearance. NSCLC accounts for 80% of lung cancers. NSCLC is divided into three major histological subtypes, including adenocarcinoma (AC), squamous cell carcinoma (SCC), and large cell carcinoma (LCC) [4]. Lung SCC is the second most frequent type of NSCLC after lung AC [5]. In recent years, molecular target therapies for lung AC, including tyrosine kinase inhibitor (gefitinib/erlotinib) against EGFR-sensitive mutants [6,7], crizotinib against ALK fusion [8], and bevacizumab against VEGF over-expression [9], have shown remarkable therapeutic efficacy. However, there is no currently approved molecular target therapy for treatment of lung SCC other than chemotherapy [10–12].

Currently, the pathogenesis mechanism of lung SCC remains unclear. It is reported that dysregulated genes, dysregulated miRNAs, and aberrantly methylated genes are associated with the progression of lung SCC. Hupl-1 functions as a tumor suppressor, and the reduced expression of Hupl-1 shows an inverse correlation with lung SCC progression; inhibition of Hupl-1 contributes to the progression of lung squamous cell carcinoma [13]. USP7 overexpression may regulate the survival and invasive properties of lung SCC and predict a poor prognosis of lung SCC [14]. Inhibition of the tumor-suppressive miR-29 family enhances cell invasion in lung SCC through direct regulation of oncogenic LOXL2 [15]. PRDM5 is a tumor suppressor frequently downregulated in tumors. DNA methylation of PRDM5 promoter contributes to the development of lung SCC [16].

Transcription factors function by regulating gene expression through binding to specific DNA sequences and play essential roles in cancer cell processes, including cell proliferation, apoptosis, and migration. Downregulation of transcription factor PROX1 in esophageal squamous cell carcinoma (ESCC) inhibits cellular proliferation and migration; high expression of PROX1 in ESCC could be used as an indicator of poor prognosis [17]. FOXP3 inhibition decreases cell proliferation, migration, invasion, and the secretion of inhibitory cytokines in lung AC [18].

In this study, we used bioinformatics methods to integrate mRNA expression data of lung SCC patients (which were

available on the GEO database) in order to identify DEG differences between lung SCC and normal controls. We constructed a transcription factor gene regulatory network of DEGs in lung SCC to find the key transcription factors in lung SCC. The aim of this study was to provide valuable information for further elucidation of the mechanism of pathogenesis and to identify potential therapeutic targets for lung SCC.

Material and Methods

Microarray data

The Gene Expression Omnibus (GEO, <http://www.ncbi.nlm.nih.gov/geo/>) database was retrieved in order to obtain the microarray data of lung SCC (up to January 1, 2015). The datasets including more than six lung SCC cases or controls. The inclusion criteria of datasets were set as follows: 1) the whole-genome expression profiling of lung SCC tissues or normal control tissues was available in the datasets; and 2) patients did not have preoperative treatment before collection of tumor tissues and normal controls. A total of six mRNA expression datasets of lung SCC were used in our study. Two datasets were based on a platform of GPL6480 Agilent-014850 Whole Human Genome Microarray 4x44K; other datasets were based on platforms of GPL10558 Illumina HumanHT-12 V4.0 expression beadchip, GPL6947 Illumina HumanHT-12 V3.0 expression beadchip, GPL9053 Agilent-UNC-custom-4X44K, and GPL570 [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array.

Data preprocessing

Different sequencing platforms are known to commonly cause heterogeneity among different microarray datasets, which makes it difficult to compare microarray datasets directly. To eliminate these discrepancies, the raw expression datasets were downloaded and preprocessed, and background correction and normalization was performed using R package metaMA [19]. For each gene, the expression level was calculated.

Identification of DEGs

The linear model limma [20] package for microarray data in R language was used to analyze the chip data. A *t*-test was used to identify genes expressed differently between lung SCC tumor samples and normal tissues samples. The *p* value and fold change were calculated. The *p* values from multiple studies were combined using Fisher's combined probability method. The false discovery rate (FDR) [21] was used for multiple test corrections of raw *p* values using the Benjamini and Hochberg method [22]. The threshold for the DEGs was set as FDR < 0.01.

Table 1. mRNA expression profiles of lung squamous cell carcinoma in GEO database.

GEO ID	Control	Case	Platform	Year	Author
GSE60644	12	23	GPL10558 Illumina HumanHT-12 V4.0 expression beadchip	2014	Staaf J. et al.
GSE40588	60	0	GPL6480 (Agilent-014850 Whole Human Genome Microarray 4x44K)	2014	Bangrong C. et al.
GSE33479	27	14	GPL6480 (Agilent-014850 Whole Human Genome Microarray 4x44K)	2014	Mascaux C. et al.
GSE23822	0	56	GPL6947 (Illumina HumanHT-12 V3.0 expression beadchip)	2012	Wright C.M. et al.
GSE17710	0	56	GPL9053 (Agilent-UNC-custom-4X44K)	2010	Wilkerson M.D. et al.
GSE10245	0	18	GPL570 ([HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array)	2008	Kuner R. et al.

Hierarchical clustering

Hierarchical clustering has been extensively applied to identify groups of similarly expressed genes from gene expression data. To reveal samples in which the closest groups were adjacent, a two-way hierarchical clustering analysis [23] was applied to genes using the “pheatmap” package in R language. The results were displayed using a heat map.

GO and KEGG pathway enrichment analysis of DEGs

GO analysis has commonly been used for functional studies of large-scale transcriptomics data. The KEGG pathway database contains information of gene networks [24]. GOrilla was used for GO analysis and the Database for Annotation Visualization and Integrated Discovery (DAVID) [25] was used for KEGG pathway enrichment of DEGs. The threshold of GO function and KEGG pathway of DEGs was set as $p < 0.001$ and $FDR < 0.01$, respectively.

Identification of transcription factors and targeted genes

TRANSFAC (<http://www.gene-regulation.com/pub/databases.html>) [26] provides data on eukaryotic transcription factors, and includes experimentally-proven binding sites and consensus binding sequences. Data of Position Weight Matrix (PMW), human transcription factors, and binding sites motif of transcription factors were downloaded from TRANSFAC. Based on the downloaded data, DEGs were used for screening transcription factors and obtaining transcription factor regulated genes.

Construction of transcription factor regulatory network

The identified transcription factors and target genes were used for regulatory network construction, and the network was visualized by Cytoscape software (<http://cytoscape.org/>) [27].

In this system, nodes represent transcription factors or target genes, and lines represent associations between transcription factors and target genes.

Results

Differentially expressed genes in lung SCC

We collected six mRNA expression profiles (GSE60644, GSE40588, GSE33479, GSE23822, GSE17710, and GSE10245), including 167 lung SCC cases and 99 normal controls (Table 1). After normalization of the raw microarray data, 1,011 significant DEGs were identified in lung SCC compared to normal controls, including 549 upregulated and 462 downregulated genes based on the cut-off criteria. The top 15 significantly upregulated and downregulated genes are listed in Table 2. The full list of DEGs are shown in Supplementary Table 1. The expression pattern of the top 200 significant DEGs are displayed in Figure 1.

GO annotation of DEGs in lung SCC

DEGs of lung SCC were performed using GO annotation to ascertain their biological roles. The threshold of GO terms was a p value < 0.001 . Vesicle-mediated transport (GO: 0016192, $p = 2.69 \times 10^{-12}$), regulation of multicellular organismal process (GO: 0051239, $p = 9.39 \times 10^{-10}$) and regulation of cell migration (GO: 0030334, $p = 2.25 \times 10^{-9}$) were the most significant enrichments of biological process. Molecular transducer activity (GO: 0060089, $p = 1.66 \times 10^{-13}$), receptor activity (GO: 0004872, $p = 1.67 \times 10^{-12}$) and signal transducer activity (GO: 0004871, $p = 1.49 \times 10^{-11}$) were the highest for enrichment of molecular function. Membrane part (GO: 0044425, $p = 3.30 \times 10^{-27}$), intrinsic component of membrane (GO: 0031224, $p = 1.76 \times 10^{-21}$), and integral component of membrane (GO: 0016021, $p = 4.01 \times 10^{-20}$)

Table 2. Differentially expressed genes in lung SCC.

Gene symbol	Official full name	Log ₂ FC	p-value	FDR
Up-regulation (top15)				
HOXC13	Homeobox C13	11.67608	1.11×10 ⁻⁴³	1.31×10 ⁻⁴¹
HOXD13	Homeobox D13	11.2923	2.95×10 ⁻²²	6.08×10 ⁻²¹
KRT31	Keratin 31	11.18891	1.29×10 ⁻²⁵	3.82×10 ⁻²⁴
HOXD11	Homeobox D11	11.10495	1.02×10 ⁻³⁴	6.57×10 ⁻³³
ZIC5	Zic family member 5	10.88417	5.00×10 ⁻³¹	2.33×10 ⁻²⁹
AKR1B15	Aldo-keto reductase family 1, member B15	10.8267	4.25×10 ⁻²⁸	1.56×10 ⁻²⁶
RAET1L	Retinoic acid early transcript 1L	10.7926	7.02×10 ⁻³³	3.89×10 ⁻³¹
KRTAP4-1	Keratin associated protein 4-1	10.74082	4.22×10 ⁻³⁹	3.88×10 ⁻³⁷
GNGT1	G protein subunit gamma transducin 1	10.7181	4.89×10 ⁻⁵⁹	1.29×10 ⁻⁵⁶
DLX6	Distal-less homeobox 6	10.55507	9.98×10 ⁻³³	5.48×10 ⁻³¹
C12orf56	Chromosome 12 open reading frame 56	10.50486	7.72×10 ⁻⁴⁷	1.15×10 ⁻⁴⁴
SYT14	Synaptotagmin 14	10.42359	1.39×10 ⁻²⁸	5.34×10 ⁻²⁷
PITX2	Paired like homeodomain 2	10.29313	7.09×10 ⁻²⁵	1.93×10 ⁻²³
DSG3	Desmoglein 3	10.20777	2.59×10 ⁻³⁵	1.75×10 ⁻³³
PGLYRP3	Peptidoglycan recognition protein 3	10.1229	1.11×10 ⁻²³	2.67×10 ⁻²²
Down-regulation (top 15)				
LOC149620	Chitinase, acidic pseudogene 2	-12.1594	2.40×10 ⁻²⁷	8.31×10 ⁻²⁶
CYP1A2	Cytochrome P450 family 1 subfamily A member 2	-9.76271	1.98×10 ⁻²³	4.63×10 ⁻²²
CAV3	Caveolin 3	-9.34724	3.51×10 ⁻²⁶	1.08×10 ⁻²⁴
OTC	Ornithine carbamoyltransferase	-9.08217	1.61×10 ⁻²²	3.42×10 ⁻²¹
CLDN18	Claudin 18	-8.69477	5.95×10 ⁻²⁸	2.15×10 ⁻²⁶
LOC572558	PGM5 antisense RNA 1	-8.66928	1.46×10 ⁻²⁶	4.65×10 ⁻²⁵
LCN6	Lipocalin 6	-8.61148	8.39×10 ⁻²³	1.84×10 ⁻²¹
GUCA2A	Guanylate cyclase activator 2A	-8.36433	4.32×10 ⁻²³	9.72×10 ⁻²²
GP9	Glycoprotein IX platelet	-8.36052	4.11×10 ⁻²²	8.40×10 ⁻²¹
OR6K3	Olfactory receptor family 6 subfamily K member 3	-8.17655	2.75×10 ⁻²⁹	1.13×10 ⁻²⁷
CELA2B	Chymotrypsin like elastase family member 2B	-7.98306	7.15×10 ⁻²⁷	2.36×10 ⁻²⁵
HBM	Hemoglobin subunit mu	-7.84657	1.22×10 ⁻³¹	5.96×10 ⁻³⁰
AGER	Advanced glycosylation end product-specific receptor	-7.5324	3.96×10 ⁻⁴⁶	5.57×10 ⁻⁴⁴
RXFP2	Relaxin/insulin-like family peptide receptor 2	-7.28848	4.61×10 ⁻³⁸	3.85×10 ⁻³⁶
ACSM2A	Acyl-CoA synthetase medium-chain family member 2A	-7.19524	1.04×10 ⁻²⁴	2.78×10 ⁻²³

FC – fold change; FDR – false discovery rate; lung SCC – lung squamous cell carcinoma.

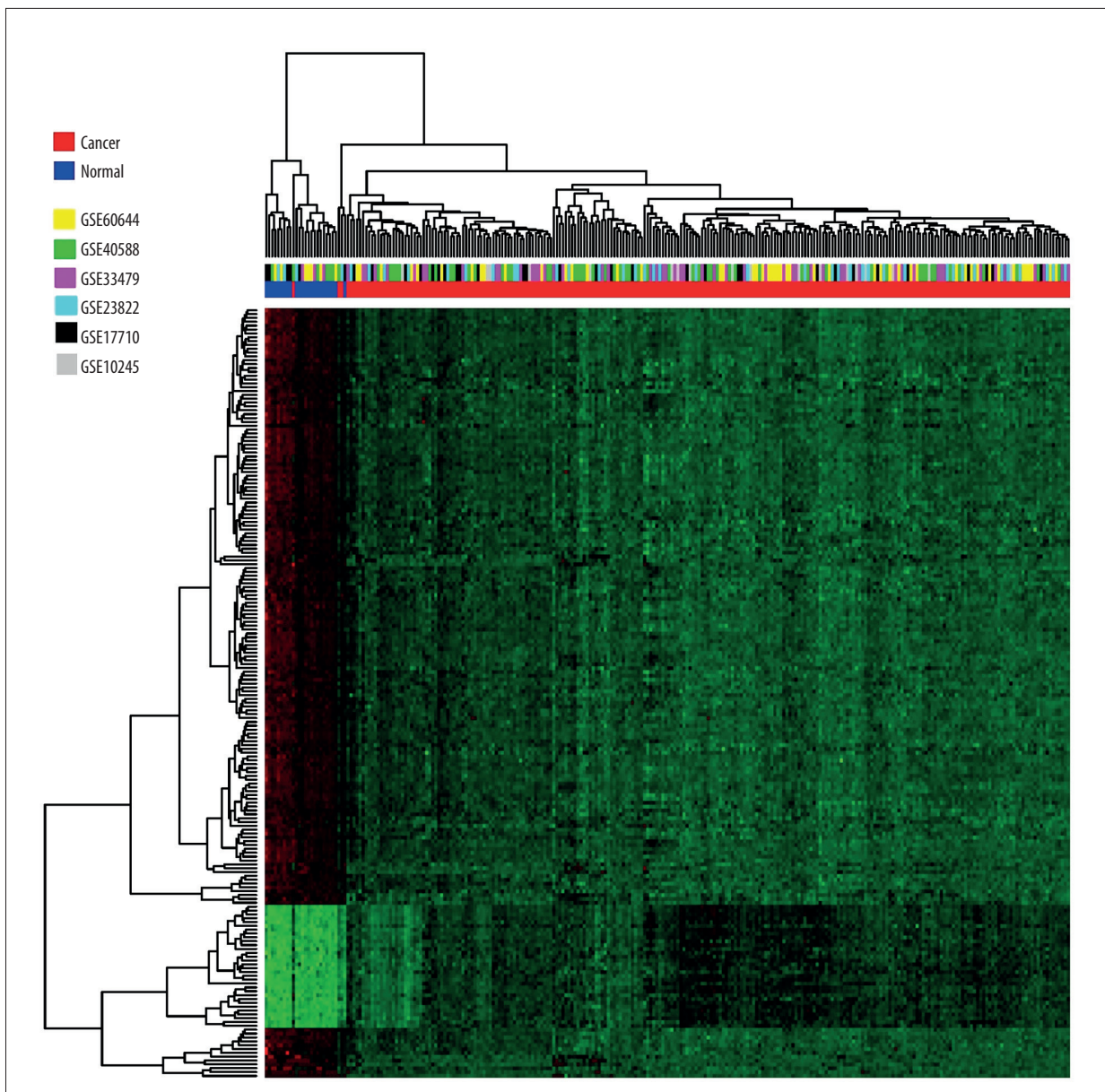


Figure 1. Heat map of differentially expressed genes in lung squamous cell carcinoma. The hierarchical clustering was performed on gene expression profiles of the top 200 DEGs between lung SCC and normal controls. Each column represents a specimen and each row represents a gene. Red color indicates genes that were upregulated and green color indicates genes that were downregulated. Black indicates genes whose expression was unchanged in tumors as compared to normal.

were the highest for enrichment of cellular components, as shown in Table 3.

KEGG pathway enrichment of DEGs in lung SCC

To obtain the signaling pathways of DEGs in lung SCC, the KEGG pathways were enriched for DEGs in lung SCC through DAVID. The threshold was FDR <0.01. The significantly enriched signaling pathways consisted of cell cycle (FDR=4.05×10⁻³⁰),

DNA replication (FDR=6.87×10⁻¹³), p53 signaling pathway (FDR=1.25×10⁻⁷), pathways in cancer (FDR=2.73×10⁻⁵), adherens junction (FDR=6.95×10⁻⁴), and cell adhesion molecules (FDR=6.95×10⁻⁴), as shown in Table 4. There were 38, 14, 13, 23, and 12 DEGs enriched in cell cycle, DNA replication, p53 signaling pathway, pathways in cancer, and cell adhesion molecules, respectively.

Table 3. GO terms of DEGs in lung SCC (top 15).

GO ID	GO terms	p-value	FDR
Biological process			
GO: 0016192	Vesicle-mediated transport	2.69×10 ⁻¹²	1.64×10 ⁻⁸
GO: 0051239	Regulation of multicellular organismal process	9.39×10 ⁻¹⁰	2.85×10 ⁻⁶
GO: 0030334	Regulation of cell migration	2.25×10 ⁻⁹	4.56×10 ⁻⁶
GO: 2000145	Regulation of cell motility	2.47×10 ⁻⁹	3.75×10 ⁻⁶
GO: 0045765	Regulation of angiogenesis	2.67×10 ⁻⁹	3.25×10 ⁻⁶
GO: 1901342	Regulation of vasculature development	3.89×10 ⁻⁹	3.94×10 ⁻⁶
GO: 0040012	Regulation of locomotion	4.95×10 ⁻⁹	4.30×10 ⁻⁶
GO: 0002682	Regulation of immune system process	6.04×10 ⁻⁹	4.59×10 ⁻⁶
GO: 0051270	Regulation of cellular component movement	9.70×10 ⁻⁹	6.55×10 ⁻⁶
GO: 0006897	Endocytosis	9.86×10 ⁻⁹	5.99×10 ⁻⁶
GO: 0044765	Single-organism transport	1.04×10 ⁻⁸	5.76×10 ⁻⁶
GO: 0030155	Regulation of cell adhesion	1.08×10 ⁻⁸	5.49×10 ⁻⁶
GO: 0048583	Regulation of response to stimulus	1.74×10 ⁻⁸	8.16×10 ⁻⁶
GO: 0007166	Cell surface receptor signaling pathway	2.25×10 ⁻⁸	9.75×10 ⁻⁶
GO: 0006810	Transport	2.68×10 ⁻⁸	1.09×10 ⁻⁵
Molecular function			
GO: 0060089	Molecular transducer activity	1.66×10 ⁻¹³	2.30×10 ⁻¹⁰
GO: 0004872	Receptor activity	1.67×10 ⁻¹²	1.15×10 ⁻⁹
GO: 0004871	Signal transducer activity	1.49×10 ⁻¹¹	6.85×10 ⁻⁹
GO: 0038023	Signaling receptor activity	1.52×10 ⁻¹⁰	5.27×10 ⁻⁸
GO: 0004888	Transmembrane signaling receptor activity	6.44×10 ⁻¹⁰	1.78×10 ⁻⁷
GO: 0008201	Heparin binding	9.92×10 ⁻⁷	2.29×10 ⁻⁴
GO: 1901681	Sulfur compound binding	2.00×10 ⁻⁶	3.96×10 ⁻⁴
GO: 0005539	Glycosaminoglycan binding	6.45×10 ⁻⁶	1.12×10 ⁻³
GO: 0005102	Receptor binding	1.18×10 ⁻⁵	1.82×10 ⁻³
GO: 0008289	Lipid binding	1.78×10 ⁻⁵	2.47×10 ⁻³
GO: 0004930	G-protein coupled receptor activity	2.25×10 ⁻⁵	2.83×10 ⁻³
GO: 0005178	Integrin binding	3.73×10 ⁻⁵	4.30×10 ⁻³
GO: 0005344	Oxygen transporter activity	7.34×10 ⁻⁵	7.82×10 ⁻³
GO: 0019825	Oxygen binding	7.34×10 ⁻⁵	7.26×10 ⁻³
GO: 0020037	Heme binding	1.74×10 ⁻⁴	1.61×10 ⁻²

Table 3 continued. GO terms of DEGs in lung SCC (top 15).

GO ID	GO terms	p-value	FDR
Cellular component			
GO: 0044425	Membrane part	3.39×10 ⁻²⁷	2.56×10 ⁻²⁴
GO: 0031224	Intrinsic component of membrane	1.76×10 ⁻²¹	6.64×10 ⁻¹⁹
GO: 0016021	Integral component of membrane	4.01×10 ⁻²⁰	1.01×10 ⁻¹⁷
GO: 0005886	Plasma membrane	9.98×10 ⁻¹⁹	1.88×10 ⁻¹⁶
GO: 0044459	Plasma membrane part	4.64×10 ⁻¹⁴	7.00×10 ⁻¹²
GO: 0031226	Intrinsic component of plasma membrane	7.88×10 ⁻¹³	9.90×10 ⁻¹¹
GO: 0005887	Integral component of plasma membrane	2.02×10 ⁻¹²	2.17×10 ⁻¹⁰
GO: 0016020	Membrane	2.16×10 ⁻¹¹	2.04×10 ⁻⁹
GO: 0044433	Cytoplasmic vesicle part	1.18×10 ⁻⁷	9.92×10 ⁻⁶
GO: 0009986	Cell surface	2.03×10 ⁻⁷	1.53×10 ⁻⁵
GO: 0031090	Organelle membrane	3.75×10 ⁻⁷	2.57×10 ⁻⁵
GO: 0098805	Whole membrane	4.60×10 ⁻⁷	2.89×10 ⁻⁵
GO: 0031012	Extracellular matrix	6.73×10 ⁻⁷	3.90×10 ⁻⁵
GO: 0098588	Bounding membrane of organelle	3.05×10 ⁻⁶	1.64×10 ⁻⁴
GO: 0031982	Vesicle	4.19×10 ⁻⁶	2.11×10 ⁻⁴

FDR – false discovery rate; lung SCC – lung squamous cell carcinoma.

Table 4. KEGG enrichment analysis of DEGs in lung SCC (top 15).

KEGG ID	KEGG terms	p-value	FDR	Count of No.
hsa04110	Cell cycle	2.18E-32	4.05E-30	38
hsa04114	Oocyte meiosis	5.3E-15	4.93E-13	22
hsa03030	DNA replication	1.11E-14	6.87E-13	14
hsa04115	p53 signaling pathway	2.68E-9	1.25E-7	13
hsa04914	Progesterone-mediated oocyte maturation	4.86E-9	1.81E-7	14
hsa00230	Purine metabolism	7.66E-8	2.37E-6	17
hsa05200	Pathways in cancer	1.03E-6	2.73E-5	23
hsa03440	Homologous recombination	2.54E-5	5.91E-4	6
hsa04520	Adherens junction	3.53E-5	6.95E-4	9
hsa04514	Cell adhesion molecules (CAMs)	3.74E-5	6.95E-4	12
hsa04270	Vascular smooth muscle contraction	4.26E-5	7.21E-4	11
hsa00240	Pyrimidine metabolism	5.43E-5	8.42E-4	10
hsa04330	Notch signaling pathway	6.46E-5	9.24E-4	7
hsa03430	Mismatch repair	1.15E-4	1.52E-3	5
hsa04610	Complement and coagulation cascades	1.22E-4	1.52E-3	8

FDR – false discovery rate; lung SCC – lung squamous cell carcinoma.

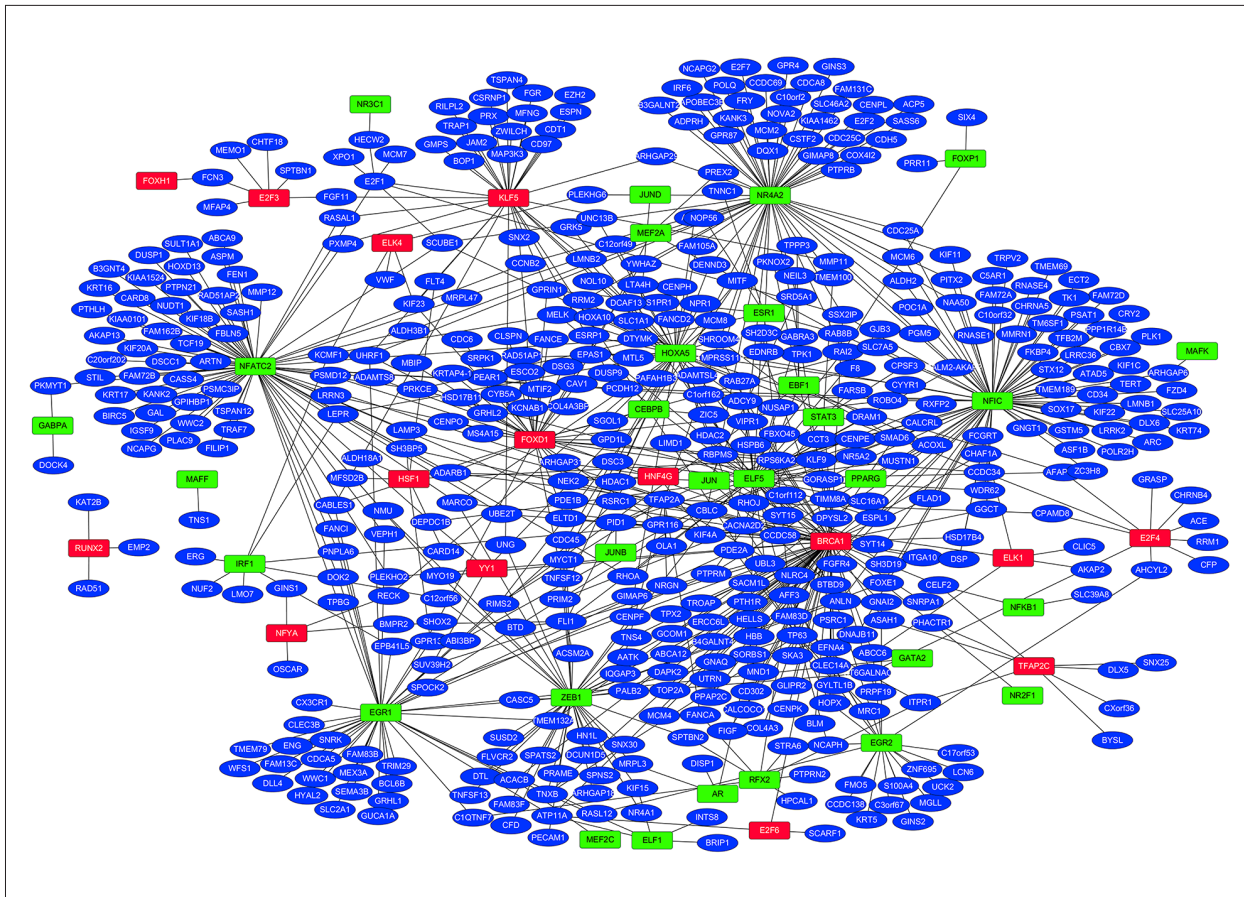


Figure 2. The transcription factor gene regulatory network of lung SCC. Green and red rectangle nodes represent downregulated and upregulated transcription factors, respectively. Blue circular nodes represent DEGs. Solid lines represent regulatory correlation between transcription factors and DEGs.

Construction of transcription factor gene regulatory network

Based on the TRANSFAC database, a total of 57 transcription factors and corresponding target genes were identified in the lung SCC-associated DEGs, including 20 upregulated transcription factors and 37 downregulated transcription factors. The 57 transcription factors and target genes were used to construct a regulatory network using Cytoscape software, as shown in Figure 2: red and green circular nodes represented upregulated and downregulated transcription factors, respectively; blue circular nodes represented DEGs; lines represented the regulatory correlations between transcription factors and DEGs. The transcription factor gene network consisted of 736 interactions between 49 transcription factors and 486 DEGs. The top 10 transcription factors that regulated DEGs the most were NFIC, BRCA1, NFATC2, NR4A2, EGR1, ELF5, HOXA5, FOXD1, ZEB1, and KLF5, as shown in Supplementary Table 2.

Discussion

In our study, NFIC regulated 83 DEGs and had the highest connectivity with DEGs in lung SCC. The expression level of NFIC was significantly downregulated in lung SCC compared to normal controls. NFIC regulated three of the top 15 upregulated genes, including GNGT1, DLX6, and PITX2 (Supplementary Table 2, Figure 2). NFIC has been shown to encode nuclear factor I/C, which belongs to the CTF/NF-I family. It has been reported that NFIC is associated with the tumor genesis of breast cancer, gastric cancer, and glioma [28–30]. NFIC is downregulated in invasive and noninvasive breast cancer cells compared to normal breast epithelial cells. Over-expression of NFIC induces expression of E-cadherin and KLF4 in breast cancer, which maintains epithelial differentiation status, leads to inhibition of EMT, and migration and invasion in breast cancer cells [30]. Recent reports suggest NFIC is dysregulated in gastric cancer. The NFI family has been shown to regulate the expression of B-FABP and GFAP, and results in increases in cell migration and anaplasia in malignant glioma cells [28]. NFIC has not previously been reported to be related to lung SCC. In

our study, NFIC was a key transcription factor in the regulatory network (Figure 2), which indicates that NFIC might contribute to the pathogenesis of lung SCC. The biological function of NFIC in lung SCC needs to be further elucidated.

In our study, BRCA1 had the second highest connectivity with DEGs, and it regulated 82 DEGs in the regulatory network (Supplementary Table 2, Figure 2). BRCA1 was significantly upregulated in lung SCC compared to normal controls. BRCA1 is known to encode the breast cancer 1 gene and act as a tumor suppressor. Mutations in this gene are responsible for approximately 40% of inherited breast cancers and 80% of inherited ovarian cancers [31]. Mounting evidence shows that the expression of BRCA1 is associated with the natural prognosis and treatment prognosis in lung cancer [32,33]. High levels of BRCA1 and SETDB1 expression have been significantly associated with shorter disease-free survival in stage I NSCLC patients [33]. NSCLC patients lacking the expression of ERCC1 and BRCA1 benefit more from adjuvant cisplatin-based chemotherapy compared with patients that expressed either ERCC1 or BRCA1 [32]. All of the aforementioned suggests that BRCA1 might play a vital role in cell proliferation, motility, and invasion of NSCLC.

In our study, NFATC2 regulated 75 DEGs in the regulatory network (Supplementary Table 2, Figure 2) and had the third highest connectivity with DEGs. NFATC2 was downregulated in lung SCC compared to normal controls. The second top upregulated gene (Table 2), HOXD13, was regulated by NFATC2. NFATC2 is known to encode the nuclear factor of activated T-cells, cytoplasmic, and calcineurin-dependent 2, which is a member of the nuclear factor of activated T cells family. NFATC2 is considered to be involved in the development of cardiac, skeletal muscle, nervous system, and tumor genesis. NFATC2 contributes to the development of breast cancer, colon cancer, and lung cancer [34–37]. In the experimental model, NFATC2-deficient mice with colitis were protected from colorectal carcinoma development, in contrast to wild-type BALB/c mice [34].

Moreover, NFATC2 has been shown to promote the migration and invasion of breast cancer cells *in vitro* [36]. In breast cancer, NFATC2-mediated IL8 production promotes the migration of primary human neutrophils *in vitro*, and promotes neutrophil infiltration in tumor xenografts and suppresses tumor growth [37]. NFATC2 is known to be overexpressed in lung cancer, and depleting the expression of NFATC2 in NSCLC cells can inhibit cell invasion, migration, and metastasis. In our study, NFATC2 was downregulated in lung SCC, the biological functions of NFATC2 in the development of lung SCC were unclear, and the underlying mechanism of action needs further study.

A total of 1,011 DEGs were identified in lung SCC compared to normal controls. All of the DEGs were significantly enriched in several KEGG pathways, including cell cycle, DNA replication, p53 signaling pathway, pathways in cancer, adherens junction, and cell adhesion molecules (Table 4). It has been previously reported that cell cycle and DNA replication is significantly enriched in lung SCC [38], which is accordance with our analysis.

Conclusions

We identified 1,011 DEGs, including 549 upregulated genes and 462 downregulated genes, in lung SCC. Transcription factors of lung SCC were identified and assays performed to construct a transcription factor regulatory network. In this network, we found several transcription factors, including NFIC, BRCA1, and NFATC2, which may play important roles in lung SCC via cell cycle and DNA replication signaling pathways. Our findings might provide valuable information for additional pathogenesis elucidation of lung SCC. Moreover, our study revealed that NFIC, BRCA1, and NFATC2 might be clinically useful if tested further for their therapeutic value.

Conflict of interest statement

All of the authors declare that they have no conflict of interest.

Supplementary Tables

Supplementary Table 1. The full list of DEGs in lung SCC.

Gene symbol	Log ₂ FC	p-value	FDR
Up-regulation			
HOXC13	11.67608	1.11×10 ⁻⁴³	1.31×10 ⁻⁴¹
HOXD13	11.2923	2.95×10 ⁻²²	6.08×10 ⁻²¹
KRT31	11.18891	1.29×10 ⁻²⁵	3.82×10 ⁻²⁴
HOXD11	11.10495	1.02×10 ⁻³⁴	6.57×10 ⁻³³
ZIC5	10.88417	5.00×10 ⁻³¹	2.33×10 ⁻²⁹
AKR1B15	10.8267	4.25×10 ⁻²⁸	1.56×10 ⁻²⁶

Gene symbol	Log ₂ FC	p-value	FDR
RAET1L	10.7926	7.02×10 ⁻³³	3.89×10 ⁻³¹
KRTAP4-1	10.74082	4.22×10 ⁻³⁹	3.88×10 ⁻³⁷
GNGT1	10.7181	4.89×10 ⁻³⁹	1.29×10 ⁻⁵⁶
DLX6	10.55507	9.98×10 ⁻³³	5.48×10 ⁻³¹
C12orf56	10.50486	7.72×10 ⁻⁴⁷	1.15×10 ⁻⁴⁴
SYT14	10.42359	1.39×10 ⁻²⁸	5.34×10 ⁻²⁷
PITX2	10.29313	7.09×10 ⁻²⁵	1.93×10 ⁻²³
DSG3	10.20777	2.59×10 ⁻³⁵	1.75×10 ⁻³³
PGLYRP3	10.1229	1.11×10 ⁻²³	2.67×10 ⁻²²
TMPRSS11F	10.0573	4.58×10 ⁻²³	1.03×10 ⁻²¹
CST4	10.00451	1.43×10 ⁻²⁹	5.98×10 ⁻²⁸
BARX1	9.786584	3.05×10 ⁻²⁴	7.81×10 ⁻²³
HOXA13	9.768895	4.28×10 ⁻²⁶	1.31×10 ⁻²⁴
CALML3	9.676866	2.86×10 ⁻²⁶	8.86×10 ⁻²⁵
DLX6AS	9.607812	8.04×10 ⁻³⁰	3.42×10 ⁻²⁸
KRT6C	9.49044	9.95×10 ⁻³⁸	8.11×10 ⁻³⁶
USH1G	9.356453	1.93×10 ⁻³⁴	1.22×10 ⁻³²
TERT	9.302319	5.49×10 ⁻³⁹	4.99×10 ⁻³⁷
C5orf46	9.247633	3.62×10 ⁻³³	2.08×10 ⁻³¹
KRT6A	9.175738	1.62×10 ⁻³⁷	1.31×10 ⁻³⁵
AKR1B10	9.050792	7.46×10 ⁻²³	1.64×10 ⁻²¹
KRT74	9.024361	2.30×10 ⁻²⁶	7.16×10 ⁻²⁵
KRT16	8.990361	3.06×10 ⁻³³	1.78×10 ⁻³¹
SPERT	8.966005	1.20×10 ⁻³⁵	8.41×10 ⁻³⁴
GABRA3	8.930546	3.48×10 ⁻³⁵	2.32×10 ⁻³³
KRT6B	8.894916	1.35×10 ⁻³⁴	8.59×10 ⁻³³
LOC339674	8.840581	8.47×10 ⁻⁴⁸	1.31×10 ⁻⁴⁵
GABRQ	8.765659	9.34×10 ⁻²³	2.03×10 ⁻²¹
IL1F5	8.758793	1.98×10 ⁻²²	4.16×10 ⁻²¹
ZIC2	8.684894	6.98×10 ⁻³³	3.87×10 ⁻³¹
PRAME	8.615422	5.36×10 ⁻²⁴	1.35×10 ⁻²²
SERPINB5	8.384097	2.04×10 ⁻⁵²	4.15×10 ⁻⁵⁰
GJB6	8.340988	6.15×10 ⁻²⁷	2.05×10 ⁻²⁵
DLL3	8.234224	2.29×10 ⁻²⁵	6.62×10 ⁻²⁴
FOXE1	8.228793	4.91×10 ⁻²⁴	1.24×10 ⁻²²
NMU	8.096627	6.08×10 ⁻²⁵	1.66×10 ⁻²³
PNCK	8.087377	1.21×10 ⁻³¹	5.93×10 ⁻³⁰
ABCA12	7.947086	1.81×10 ⁻³⁷	1.46×10 ⁻³⁵
LOC642587	7.735536	1.09×10 ⁻³⁵	7.66×10 ⁻³⁴
FAM131C	7.695912	2.95×10 ⁻³⁵	1.98×10 ⁻³³
FOXD3	7.665217	5.47×10 ⁻²⁴	1.37×10 ⁻²²
DVWA	7.626607	2.90×10 ⁻³⁰	1.28×10 ⁻²⁸
DQX1	7.587993	6×10 ⁻⁴⁴	7.37×10 ⁻⁴²

Gene symbol	Log ₂ FC	p-value	FDR
KRT5	7.513929	2.84×10 ⁻²⁶	8.78×10 ⁻²⁵
DUSP9	7.338712	2.55×10 ⁻³⁸	2.17×10 ⁻³⁶
GUCA1A	7.312747	1.47×10 ⁻²⁷	5.14×10 ⁻²⁶
PITX1	7.178973	2.40×10 ⁻⁵¹	4.65×10 ⁻⁴⁹
GRHL3	7.163425	5.74×10 ⁻³⁹	5.19×10 ⁻³⁷
CA9	7.14797	2.94×10 ⁻²²	6.07×10 ⁻²¹
COL11A1	7.114174	5.99×10 ⁻²⁹	2.40×10 ⁻²⁷
GPR87	7.058347	7.88×10 ⁻⁴⁰	7.53×10 ⁻³⁸
RAB3B	6.975845	3.58×10 ⁻²⁵	1.01×10 ⁻²³
GAL	6.972401	1.87×10 ⁻²³	4.38×10 ⁻²²
RIMS2	6.912368	5.50×10 ⁻²⁴	1.38×10 ⁻²²
DSC3	6.790565	9.81×10 ⁻²⁹	3.83×10 ⁻²⁷
RAD51AP2	6.760157	1.20×10 ⁻²²	2.58×10 ⁻²¹
FAM83B	6.682755	3.54×10 ⁻⁴⁴	4.43×10 ⁻⁴²
RDM1	6.680239	1.56×10 ⁻⁴²	1.71×10 ⁻⁴⁰
HIST1H2BH	6.676184	3.21×10 ⁻³⁴	1.98×10 ⁻³²
KRT17	6.482533	4.25×10 ⁻²⁷	1.44×10 ⁻²⁵
B4GALNT4	6.378898	5.07×10 ⁻³⁹	4.63×10 ⁻³⁷
FAT2	6.252899	3.61×10 ⁻²⁷	1.24×10 ⁻²⁵
NXPH4	6.161888	4.61×10 ⁻⁴²	4.88×10 ⁻⁴⁰
UCN2	6.083164	5.41×10 ⁻²⁶	1.64×10 ⁻²⁴
COL7A1	6.069926	8.58×10 ⁻³⁴	5.09×10 ⁻³²
MMP12	6.043639	3.19×10 ⁻³⁶	2.35×10 ⁻³⁴
CHRNB4	6.038051	1.51×10 ⁻²⁴	3.99×10 ⁻²³
S100A2	6.034598	9.51×10 ⁻²⁵	2.56×10 ⁻²³
FAM83F	5.987037	1.53×10 ⁻⁴⁵	2.08×10 ⁻⁴³
OTX1	5.913971	1.71×10 ⁻³⁶	1.29×10 ⁻³⁴
PTHLH	5.911066	5.97×10 ⁻²⁴	1.49×10 ⁻²²
GJB5	5.910018	1.73×10 ⁻²⁸	6.59×10 ⁻²⁷
TFAP2A	5.898686	1.99×10 ⁻⁵⁷	4.75×10 ⁻⁵⁵
ZNF695	5.857676	3.04×10 ⁻²⁴	7.81×10 ⁻²³
PPP2R2C	5.84455	9.58×10 ⁻²⁴	2.32×10 ⁻²²
KREMEN2	5.813638	1.98×10 ⁻²³	4.62×10 ⁻²²
DLX5	5.743708	1.04×10 ⁻³¹	5.16×10 ⁻³⁰
KRT15	5.703738	2.04×10 ⁻²²	4.27×10 ⁻²¹
TMPRSS4	5.681538	8.78×10 ⁻³¹	4.03×10 ⁻²⁹
SLC2A1	5.608247	1.03×10 ⁻⁶¹	3.20×10 ⁻³⁹
SHOX2	5.540305	5.29×10 ⁻³⁰	2.28×10 ⁻²⁸
TNS4	5.489393	2.16×10 ⁻²⁸	8.16×10 ⁻²⁷
NKAIN1	5.44417	1.62×10 ⁻²⁵	4.76×10 ⁻²⁴
CDC45	5.396202	5.31×10 ⁻⁷⁴	6.82×10 ⁻⁷¹
CASKIN1	5.394552	4.73×10 ⁻²³	1.06×10 ⁻²¹
GJB2	5.375627	1.68×10 ⁻²⁵	4.94×10 ⁻²⁴

Gene symbol	Log ₂ FC	p-value	FDR
MMP11	5.30769	5.44×10 ⁻³²	2.80×10 ⁻³⁰
TP63	5.275353	2.11×10 ⁻²³	4.91×10 ⁻²²
BIRC5	5.262464	6.28×10 ⁻⁷⁵	1.07×10 ⁻⁷¹
RASAL1	5.236534	2.17×10 ⁻³⁴	1.36×10 ⁻³²
TTK	5.184575	1.93×10 ⁻⁷⁴	2.82×10 ⁻⁷¹
HOXA10	5.180499	3.17×10 ⁻²⁸	1.18×10 ⁻²⁶
CENPA	5.158077	6.59×10 ⁻⁷⁴	7.96×10 ⁻⁷¹
DEPDC1	5.154545	5.80×10 ⁻⁷⁷	1.68×10 ⁻⁷³
MYBL2	5.148039	1.16×10 ⁻⁷⁰	9.50×10 ⁻⁶⁸
TROAP	5.13211	1.71×10 ⁻⁷⁴	2.70×10 ⁻⁷¹
KIF18B	5.131483	1.42×10 ⁻⁶⁸	8.84×10 ⁻⁶⁶
WDR72	5.108763	4.78×10 ⁻²⁵	1.32×10 ⁻²³
UBE2C	5.10166	1.60×10 ⁻⁷⁷	5.46×10 ⁻⁷⁴
NEK2	5.090834	2.01×10 ⁻⁷⁸	1.37×10 ⁻⁷⁴
NEIL3	5.08459	1.45×10 ⁻⁴⁶	2.09×10 ⁻⁴⁴
KIF4A	5.053856	7.81×10 ⁻⁸¹	1.60×10 ⁻⁷⁶
LYPD3	5.046497	3.12×10 ⁻³⁰	1.38×10 ⁻²⁸
POLQ	4.995522	2.51×10 ⁻⁶⁴	9.90×10 ⁻⁶²
TMEM40	4.975923	2.30×10 ⁻²⁶	7.16×10 ⁻²⁵
RHOV	4.970518	8.12×10 ⁻³⁶	5.79×10 ⁻³⁴
HJURP	4.947107	1.74×10 ⁻⁸⁰	1.78×10 ⁻⁷⁶
DLGAP5	4.944602	1.58×10 ⁻⁶⁹	1.12×10 ⁻⁶⁶
BUB1B	4.939296	1.27×10 ⁻⁷⁷	5.23×10 ⁻⁷⁴
NUF2	4.928634	1.70×10 ⁻⁷¹	1.52×10 ⁻⁶⁸
TRIM29	4.926113	3.76×10 ⁻²⁵	1.05×10 ⁻²³
KIF14	4.915327	6.74×10 ⁻⁶⁹	4.33×10 ⁻⁶⁶
TPX2	4.886094	3.20×10 ⁻⁷⁸	1.64×10 ⁻⁷⁴
STRA6	4.883579	2.73×10 ⁻²⁵	7.79×10 ⁻²⁴
EXO1	4.874045	3.73×10 ⁻⁷⁴	5×10 ⁻⁷¹
E2F7	4.867589	6.83×10 ⁻³⁹	1.78×10 ⁻⁵⁶
SPC24	4.8509	1.66×10 ⁻⁴¹	1.71×10 ⁻³⁹
MELK	4.846198	3.13×10 ⁻⁶⁶	1.49×10 ⁻⁶³
AURKB	4.841481	6.30×10 ⁻⁶⁷	3.32×10 ⁻⁶⁴
CDC20	4.832898	1.82×10 ⁻⁷⁶	3.75×10 ⁻⁷³
CDC25C	4.812971	2.43×10 ⁻⁶⁴	9.77×10 ⁻⁶²
GJB3	4.794771	1.60×10 ⁻²⁶	5.07×10 ⁻²⁵
ALG1L	4.783708	3.24×10 ⁻³⁶	2.38×10 ⁻³⁴
FOXM1	4.758629	2.36×10 ⁻⁶⁴	9.71×10 ⁻⁶²
CTSL2	4.755756	8.30×10 ⁻⁴⁴	9.85×10 ⁻⁴²
DEPDC1B	4.727546	9.84×10 ⁻⁶⁵	4.21×10 ⁻⁶²
FGF11	4.715897	4.72×10 ⁻⁴¹	4.71×10 ⁻³⁹
RAD54L	4.714778	1.81×10 ⁻⁷¹	1.54×10 ⁻⁶⁸
ARTN	4.706166	1.57×10 ⁻²⁸	6.00×10 ⁻²⁷

Gene symbol	Log ₂ FC	p-value	FDR
IGSF9	4.696405	3.38×10 ⁻⁴³	3.81×10 ⁻⁴¹
TOP2A	4.664592	1.28×10 ⁻⁶⁷	7.76×10 ⁻⁶⁵
PBK	4.647067	5.53×10 ⁻⁶⁰	1.60×10 ⁻⁵⁷
EPR1	4.615642	1.28×10 ⁻⁶²	4.70×10 ⁻⁶⁰
ANLN	4.591799	2.46×10 ⁻⁶⁷	1.36×10 ⁻⁶⁴
KIF2C	4.59067	1.31×10 ⁻⁷⁶	2.99×10 ⁻⁷³
C15orf42	4.583778	4.02×10 ⁻⁵⁶	9.07×10 ⁻⁵⁴
SLC44A5	4.575648	1.71×10 ⁻²⁵	5.02×10 ⁻²⁴
ASPM	4.558095	2.41×10 ⁻⁶²	8.49×10 ⁻⁶⁰
MCM10	4.534639	2.73×10 ⁻⁶⁶	1.33×10 ⁻⁶³
CDCA3	4.510427	4.04×10 ⁻⁷²	4.36×10 ⁻⁶⁹
SKA1	4.503986	5.42×10 ⁻⁶²	1.79×10 ⁻³⁹
PKMYT1	4.50008	3.21×10 ⁻⁶⁰	9.42×10 ⁻⁵⁸
CCNB2	4.496625	5.08×10 ⁻⁷²	5.22×10 ⁻⁶⁹
PSAT1	4.454087	1.18×10 ⁻⁵⁰	2.18×10 ⁻⁴⁸
FAM64A	4.448949	2.95×10 ⁻⁵⁸	7.29×10 ⁻⁵⁶
CKAP2L	4.419661	7.55×10 ⁻⁷²	7.38×10 ⁻⁶⁹
NCAPH	4.405723	1.02×10 ⁻⁷¹	9.52×10 ⁻⁶⁹
MND1	4.363921	1.40×10 ⁻³⁹	3.89×10 ⁻⁵⁷
C9orf140	4.353878	3.33×10 ⁻⁵⁰	5.99×10 ⁻⁴⁸
CENPF	4.346762	5.06×10 ⁻⁵⁷	1.17×10 ⁻⁵⁴
B3GNT4	4.327802	5.06×10 ⁻²⁵	1.40×10 ⁻²³
TRIP13	4.317994	2.00×10 ⁻⁶⁷	1.14×10 ⁻⁶⁴
GTSE1	4.312917	1.61×10 ⁻⁶⁴	6.74×10 ⁻⁶²
NKPD1	4.303465	3.33×10 ⁻²⁸	1.24×10 ⁻²⁶
CEP55	4.284965	2.79×10 ⁻⁶⁵	1.25×10 ⁻⁶²
SGOL1	4.284447	1.14×10 ⁻⁶⁵	5.21×10 ⁻⁶³
UHRF1	4.282768	2.52×10 ⁻³⁹	6.89×10 ⁻⁵⁷
SKA3	4.277808	3.24×10 ⁻⁶⁹	2.15×10 ⁻⁶⁶
NDC80	4.26936	8.77×10 ⁻⁶¹	2.65×10 ⁻⁵⁸
PLK1	4.263159	6.53×10 ⁻⁷⁷	1.68×10 ⁻⁷³
CDCA2	4.259662	1.43×10 ⁻⁵⁸	3.62×10 ⁻⁵⁶
C16orf59	4.220699	7.47×10 ⁻⁶⁰	2.13×10 ⁻⁵⁷
CDC6	4.214385	1.59×10 ⁻⁶²	5.72×10 ⁻⁶⁰
ALDH3B2	4.176655	4.58×10 ⁻²⁵	1.27×10 ⁻²³
PVRL1	4.17206	1.62×10 ⁻³⁵	1.12×10 ⁻³³
SLC6A8	4.167839	7.32×10 ⁻³⁴	4.38×10 ⁻³²
EPN3	4.154454	1.28×10 ⁻³⁷	1.04×10 ⁻³⁵
DSP	4.139318	2.57×10 ⁻⁴⁷	3.88×10 ⁻⁴⁵
KIF15	4.131404	2.94×10 ⁻⁵⁶	6.70×10 ⁻⁵⁴
CENPI	4.118732	1.88×10 ⁻⁵⁸	4.71×10 ⁻⁵⁶
RRM2	4.115026	3.67×10 ⁻³⁹	9.92×10 ⁻⁵⁷
ORC6L	4.096011	2.35×10 ⁻⁶⁶	1.17×10 ⁻⁶³

Gene symbol	Log ₂ FC	p-value	FDR
ESPL1	4.086499	7.36×10 ⁻⁶²	2.32×10 ⁻³⁹
OIP5	4.078864	4.35×10 ⁻⁶²	1.49×10 ⁻³⁹
PTTG3P	4.073075	2.83×10 ⁻³²	1.49×10 ⁻³⁰
CDC45	4.067312	1.39×10 ⁻⁷⁵	2.60×10 ⁻⁷²
SPC25	4.046998	2.44×10 ⁻⁶²	8.49×10 ⁻⁶⁰
KIF20A	4.017253	7.31×10 ⁻⁶³	2.73×10 ⁻⁶⁰
GINS1	4.011587	3.78×10 ⁻⁶³	1.46×10 ⁻⁶⁰
RECQL4	3.976634	1.46×10 ⁻⁵²	2.99×10 ⁻⁵⁰
FERMT1	3.968932	5.24×10 ⁻³⁴	3.14×10 ⁻³²
KIF23	3.968213	2.22×10 ⁻⁷³	2.53×10 ⁻⁷⁰
NCAPG	3.965541	2.62×10 ⁻⁶⁹	1.80×10 ⁻⁶⁶
CCNA2	3.960237	1.14×10 ⁻⁶⁵	5.21×10 ⁻⁶³
KIF4B	3.955288	2.41×10 ⁻³⁵	1.63×10 ⁻³³
FAM83D	3.941613	7.25×10 ⁻⁴⁹	1.18×10 ⁻⁴⁶
ORC1L	3.928708	5.44×10 ⁻⁶³	2.07×10 ⁻⁶⁰
CDT1	3.906273	3.86×10 ⁻⁵⁸	9.45×10 ⁻⁵⁶
CCNE1	3.905245	5.56×10 ⁻⁵⁰	9.76×10 ⁻⁴⁸
ERCC6L	3.901439	1.72×10 ⁻⁴⁸	2.77×10 ⁻⁴⁶
IQGAP3	3.89972	1.47×10 ⁻⁵³	3.12×10 ⁻⁵¹
E2F8	3.88784	2.90×10 ⁻⁵⁰	5.27×10 ⁻⁴⁸
ESCO2	3.886113	1.15×10 ⁻⁵⁴	2.52×10 ⁻⁵²
CDCA8	3.872866	4.11×10 ⁻⁷⁰	3.12×10 ⁻⁶⁷
C1orf135	3.853428	1.32×10 ⁻⁶⁷	7.77×10 ⁻⁶⁵
AK3L1	3.850189	6.67×10 ⁻⁴⁵	8.73×10 ⁻⁴³
KIAA0101	3.8051	1.11×10 ⁻⁴⁶	1.62×10 ⁻⁴⁴
MKI67	3.801386	4.44×10 ⁻⁴⁸	6.96×10 ⁻⁴⁶
UBE2T	3.792088	5.39×10 ⁻⁶²	1.79×10 ⁻³⁹
FBXO43	3.78562	3.26×10 ⁻³⁰	1.43×10 ⁻²⁸
CDKN3	3.771015	4.21×10 ⁻⁴⁸	6.65×10 ⁻⁴⁶
HELLS	3.744593	3.17×10 ⁻⁶⁰	9.42×10 ⁻⁵⁸
CBLC	3.729905	1.21×10 ⁻³¹	5.94×10 ⁻³⁰
KIF11	3.702491	1.11×10 ⁻⁶⁹	8.13×10 ⁻⁶⁷
XRCC2	3.692712	1.11×10 ⁻⁵⁰	2.08×10 ⁻⁴⁸
RAD51	3.678599	3.82×10 ⁻⁶⁷	2.06×10 ⁻⁶⁴
CDCA7	3.678311	7.55×10 ⁻⁴¹	7.41×10 ⁻³⁹
GINS2	3.676896	2.62×10 ⁻⁵³	5.44×10 ⁻⁵¹
BRIP1	3.664418	3.37×10 ⁻⁴⁹	5.72×10 ⁻⁴⁷
BUB1	3.653271	6.80×10 ⁻⁶²	2.21×10 ⁻³⁹
PRC1	3.633728	3.71×10 ⁻⁷⁰	2.93×10 ⁻⁶⁷
CDC25A	3.619686	9.37×10 ⁻⁶⁰	2.64×10 ⁻⁵⁷
SPAG5	3.615543	8.35×10 ⁻⁵⁴	1.80×10 ⁻⁵¹
NUSAP1	3.614775	9.72×10 ⁻⁶⁵	4.21×10 ⁻⁶²
HMMR	3.608103	5.43×10 ⁻⁵⁰	9.61×10 ⁻⁴⁸

Gene symbol	Log ₂ FC	p-value	FDR
CASC5	3.600462	9.91×10 ⁻⁵¹	1.87×10 ⁻⁴⁸
EME1	3.588628	1.21×10 ⁻⁴⁷	1.86×10 ⁻⁴⁵
CCNB1	3.582266	1.09×10 ⁻⁶⁶	5.61×10 ⁻⁶⁴
C17orf53	3.576527	2.62×10 ⁻⁵²	5.28×10 ⁻⁵⁰
ESPN	3.563273	4.19×10 ⁻²²	8.56×10 ⁻²¹
MAD2L1	3.561721	1.06×10 ⁻⁵⁸	2.73×10 ⁻⁵⁶
KIFC1	3.553172	4.27×10 ⁻³⁹	1.14×10 ⁻⁵⁶
TK1	3.50071	4.06×10 ⁻⁴⁹	6.84×10 ⁻⁴⁷
MEX3A	3.496692	6.18×10 ⁻²⁸	2.23×10 ⁻²⁶
MTL5	3.477409	5.71×10 ⁻³¹	2.64×10 ⁻²⁹
F12	3.472053	4.57×10 ⁻²⁸	1.67×10 ⁻²⁶
CENPE	3.47034	7.84×10 ⁻⁵²	1.55×10 ⁻⁴⁹
FAM72D	3.452976	7.98×10 ⁻⁴⁵	1.04×10 ⁻⁴²
CDK1	3.445157	1.90×10 ⁻⁵⁷	4.60×10 ⁻⁵⁵
ARNTL2	3.39676	6.40×10 ⁻²⁹	2.55×10 ⁻²⁷
EFNA3	3.370801	6.83×10 ⁻³⁷	5.27×10 ⁻³⁵
FAM72A	3.363086	5.21×10 ⁻⁴¹	5.16×10 ⁻³⁹
PERP	3.334142	3.30×10 ⁻⁴⁴	4.16×10 ⁻⁴²
AURKA	3.311686	3.49×10 ⁻⁶¹	1.07×10 ⁻⁵⁸
CLSPN	3.303698	5.86×10 ⁻³⁷	4.54×10 ⁻³⁵
RAD51AP1	3.297327	1.43×10 ⁻⁴⁶	2.07×10 ⁻⁴⁴
APOBEC3B	3.293181	2.23×10 ⁻²⁴	5.78×10 ⁻²³
SLC7A5	3.28233	2.96×10 ⁻²⁸	1.11×10 ⁻²⁶
GINS4	3.277009	4.18×10 ⁻⁴⁰	4.03×10 ⁻³⁸
MCM2	3.275282	1×10 ⁻⁵³	2.35×10 ⁻⁵¹
ASF1B	3.274737	4.31×10 ⁻⁴⁹	7.20×10 ⁻⁴⁷
FAM111B	3.226599	2.50×10 ⁻³⁴	1.57×10 ⁻³²
C18orf56	3.220686	1.06×10 ⁻³¹	5.21×10 ⁻³⁰
STIL	3.220046	7.31×10 ⁻⁶²	2.32×10 ⁻³⁹
CENPM	3.219859	8.77×10 ⁻⁴⁵	1.13×10 ⁻⁴²
C3orf67	3.213877	6.71×10 ⁻²⁸	2.41×10 ⁻²⁶
ZWINT	3.211688	5.80×10 ⁻⁵⁶	1.29×10 ⁻⁵³
GPR19	3.197658	1.42×10 ⁻²⁷	4.99×10 ⁻²⁶
C16orf75	3.173953	1.24×10 ⁻⁴¹	1.29×10 ⁻³⁹
FAM72B	3.165921	2.44×10 ⁻⁴⁵	3.25×10 ⁻⁴³
PRR11	3.160902	9.90×10 ⁻³⁵	6.39×10 ⁻³³
WDR62	3.156169	3.08×10 ⁻³⁵	2.06×10 ⁻³³
E2F2	3.149669	1.90×10 ⁻⁴²	2.06×10 ⁻⁴⁰
CHRNA5	3.146514	3.38×10 ⁻²⁹	1.38×10 ⁻²⁷
ECE2	3.139391	1.69×10 ⁻³⁸	1.47×10 ⁻³⁶
EZH2	3.120503	1.98×10 ⁻⁴⁶	2.83×10 ⁻⁴⁴
KIAA1524	3.117976	5.08×10 ⁻⁵²	1.01×10 ⁻⁴⁹
RFC4	3.115315	2.26×10 ⁻⁴⁶	3.20×10 ⁻⁴⁴

Gene symbol	Log ₂ FC	p-value	FDR
PIF1	3.099859	3.88×10 ⁻³³	2.21×10 ⁻³¹
PLEKHG6	3.078176	1.15×10 ⁻²⁷	4.04×10 ⁻²⁶
CARD14	3.076131	4.59×10 ⁻²³	1.03×10 ⁻²¹
C12orf48	3.071974	2.60×10 ⁻⁴²	2.80×10 ⁻⁴⁰
FANCI	3.05856	1.69×10 ⁻⁵⁵	3.72×10 ⁻⁵³
ARHGAP11A	3.057591	1.08×10 ⁻⁵¹	2.11×10 ⁻⁴⁹
PTTG1	3.056546	4.20×10 ⁻⁵⁷	9.80×10 ⁻⁵⁵
ECT2	3.037686	6.06×10 ⁻⁴⁴	7.36×10 ⁻⁴²
MLF1IP	2.98928	5.12×10 ⁻⁴³	5.74×10 ⁻⁴¹
MCM4	2.985368	4.08×10 ⁻⁵⁷	9.62×10 ⁻⁵⁵
TMEM132A	2.978913	1.13×10 ⁻³⁹	1.07×10 ⁻³⁷
POLE2	2.942741	4.82×10 ⁻³⁶	3.51×10 ⁻³⁴
CENPK	2.920134	1.95×10 ⁻³⁶	1.46×10 ⁻³⁴
BLM	2.89101	2.93×10 ⁻⁴⁵	3.88×10 ⁻⁴³
DNA2	2.86944	3.03×10 ⁻⁴³	3.43×10 ⁻⁴¹
NFKBIL2	2.864318	6.18×10 ⁻³⁵	4.06×10 ⁻³³
C5orf34	2.86051	1.45×10 ⁻³⁵	1.00×10 ⁻³³
SHCBP1	2.85255	2.05×10 ⁻⁴⁵	2.75×10 ⁻⁴³
GYLTL1B	2.851155	1.08×10 ⁻²²	2.33×10 ⁻²¹
DTL	2.84936	3.07×10 ⁻³⁸	2.61×10 ⁻³⁶
RAD54B	2.833386	8.52×10 ⁻⁵¹	1.62×10 ⁻⁴⁸
C9orf100	2.82468	2.62×10 ⁻³⁵	1.76×10 ⁻³³
UBE2S	2.803809	1.89×10 ⁻⁴²	2.06×10 ⁻⁴⁰
IRF6	2.802423	1.21×10 ⁻²⁸	4.71×10 ⁻²⁷
FANCB	2.762651	2.55×10 ⁻³⁹	2.37×10 ⁻³⁷
CCNE2	2.756919	1.49×10 ⁻³⁴	9.46×10 ⁻³³
CHEK1	2.746504	2.41×10 ⁻⁵³	5.05×10 ⁻⁵¹
MARK1	2.727147	8.69×10 ⁻²³	1.90×10 ⁻²¹
HMGA1	2.726709	1.31×10 ⁻⁴⁶	1.91×10 ⁻⁴⁴
CENPW	2.726381	7.49×10 ⁻³⁴	4.47×10 ⁻³²
GSG2	2.724667	4.49×10 ⁻³⁸	3.76×10 ⁻³⁶
PLK4	2.705375	3.47×10 ⁻⁵⁰	6.20×10 ⁻⁴⁸
SIX4	2.705223	8.25×10 ⁻³¹	3.81×10 ⁻²⁹
SPTBN2	2.698714	4.14×10 ⁻²⁶	1.27×10 ⁻²⁴
TYMS	2.682185	2.71×10 ⁻³³	1.58×10 ⁻³¹
PPAP2C	2.676826	2.01×10 ⁻²⁴	5.24×10 ⁻²³
DSCC1	2.6475	1.86×10 ⁻⁴¹	1.90×10 ⁻³⁹
ATAD5	2.623302	4.51×10 ⁻³⁴	2.74×10 ⁻³²
GPT2	2.606793	1.43×10 ⁻²⁸	5.48×10 ⁻²⁷
PYCR1	2.597461	3.14×10 ⁻²⁵	8.87×10 ⁻²⁴
CCNF	2.581834	2.80×10 ⁻⁵⁰	5.13×10 ⁻⁴⁸
DDX12	2.579215	4.42×10 ⁻²²	9.02×10 ⁻²¹
SLC16A1	2.57404	3.27×10 ⁻²⁴	8.38×10 ⁻²³

Gene symbol	Log ₂ FC	p-value	FDR
TRAIP	2.572849	9.94×10 ⁻⁴⁷	1.47×10 ⁻⁴⁴
MTBP	2.564705	4.11×10 ⁻⁴²	4.39×10 ⁻⁴⁰
TMEM79	2.542757	1.20×10 ⁻²³	2.87×10 ⁻²²
CCDC34	2.528606	4.85×10 ⁻⁴²	5.11×10 ⁻⁴⁰
FAM54A	2.527384	1.42×10 ⁻³⁵	9.86×10 ⁻³⁴
GRHL1	2.518191	2.84×10 ⁻²²	5.87×10 ⁻²¹
CDK5R1	2.504349	1.88×10 ⁻²⁵	5.48×10 ⁻²⁴
WDHD1	2.500071	7.78×10 ⁻⁴⁴	9.29×10 ⁻⁴²
CDCA4	2.497176	8.31×10 ⁻⁴¹	8.12×10 ⁻³⁹
TRIM59	2.476813	8.49×10 ⁻²⁹	3.34×10 ⁻²⁷
UCK2	2.4741	2.75×10 ⁻⁴³	3.13×10 ⁻⁴¹
GGH	2.469316	9.20×10 ⁻²⁹	3.61×10 ⁻²⁷
CENPH	2.466716	2.00×10 ⁻⁴²	2.16×10 ⁻⁴⁰
KNTC1	2.458312	2.65×10 ⁻⁴¹	2.65×10 ⁻³⁹
KPNA2	2.430685	7.10×10 ⁻⁴⁸	1×10 ⁻⁴⁵
SKP2	2.429954	2.76×10 ⁻²⁷	9.51×10 ⁻²⁶
CHAF1B	2.398405	1.87×10 ⁻³⁷	1.50×10 ⁻³⁵
KIF18A	2.379708	1.02×10 ⁻³⁴	6.57×10 ⁻³³
GPRIN1	2.37562	2.62×10 ⁻²²	5.43×10 ⁻²¹
CHTF18	2.373424	1.28×10 ⁻²⁴	3.42×10 ⁻²³
MCM8	2.358276	2.27×10 ⁻³⁸	1.95×10 ⁻³⁶
BOP1	2.356677	6.98×10 ⁻²⁵	1.90×10 ⁻²³
SRD5A1	2.355054	3.51×10 ⁻²⁸	1.30×10 ⁻²⁶
CKS1B	2.349225	1.72×10 ⁻³⁵	1.18×10 ⁻³³
RACGAP1	2.345876	2.26×10 ⁻⁴⁸	3.60×10 ⁻⁴⁶
GAPDH	2.340346	1.23×10 ⁻³⁶	9.42×10 ⁻³⁵
HMGB3	2.328465	3.03×10 ⁻²⁴	7.80×10 ⁻²³
MFSD2B	2.318549	9.42×10 ⁻²⁴	2.29×10 ⁻²²
ATAD2	2.317108	4.12×10 ⁻⁴⁴	5.09×10 ⁻⁴²
LOC100125556	2.313755	6.12×10 ⁻³³	3.42×10 ⁻³¹
C1orf74	2.286936	4.67×10 ⁻³⁰	2.02×10 ⁻²⁸
TIMELESS	2.264996	1.13×10 ⁻⁴³	1.31×10 ⁻⁴¹
RCC1	2.259865	2.44×10 ⁻³⁹	2.28×10 ⁻³⁷
C1orf112	2.259727	6.31×10 ⁻³⁸	5.16×10 ⁻³⁶
PKP3	2.249797	7.20×10 ⁻²⁷	2.37×10 ⁻²⁵
AURKAPS1	2.223938	5.47×10 ⁻²⁵	1.50×10 ⁻²³
NCAPG2	2.220921	1.22×10 ⁻³⁶	9.40×10 ⁻³⁵
ACTL6A	2.184303	1.44×10 ⁻²⁹	5.99×10 ⁻²⁸
FANCA	2.16958	7.75×10 ⁻²⁸	2.77×10 ⁻²⁶
CHEK2	2.164867	4.11×10 ⁻³¹	1.93×10 ⁻²⁹
TPBG	2.154229	3.94×10 ⁻²⁸	1.46×10 ⁻²⁶
C3orf21	2.146748	4.01×10 ⁻²⁴	1.02×10 ⁻²²
FEN1	2.137638	1.40×10 ⁻⁴²	1.55×10 ⁻⁴⁰

Gene symbol	Log ₂ FC	p-value	FDR
C11orf82	2.125601	2.15×10 ⁻²³	4.98×10 ⁻²²
PAFAH1B3	2.104472	2.15×10 ⁻²³	4.98×10 ⁻²²
DSG2	2.103021	1.34×10 ⁻²⁶	4.27×10 ⁻²⁵
FANCD2	2.102199	1.94×10 ⁻³⁸	1.68×10 ⁻³⁶
NCAPD2	2.099683	2.44×10 ⁻³⁰	1.09×10 ⁻²⁸
LOC100128191	2.096295	1.89×10 ⁻²⁸	7.19×10 ⁻²⁷
CCDC138	2.089787	4.95×10 ⁻²⁹	1.99×10 ⁻²⁷
SGOL2	2.086745	6.87×10 ⁻³⁰	2.94×10 ⁻²⁸
SLC25A10	2.084461	1.67×10 ⁻²⁷	5.82×10 ⁻²⁶
PPAT	2.074329	1.35×10 ⁻³⁶	1.03×10 ⁻³⁴
CHAF1A	2.067179	2.15×10 ⁻²⁷	7.47×10 ⁻²⁶
LMNB1	2.065592	3.32×10 ⁻³³	1.92×10 ⁻³¹
PDK1	2.063368	7.82×10 ⁻²⁹	3.09×10 ⁻²⁷
RNASEH2A	2.057419	1.27×10 ⁻³¹	6.20×10 ⁻³⁰
GMNN	2.049782	1.26×10 ⁻³¹	6.15×10 ⁻³⁰
MCM7	2.047646	7.13×10 ⁻³⁹	6.42×10 ⁻³⁷
THOC3	2.046084	7.06×10 ⁻²⁸	2.53×10 ⁻²⁶
GEMIN8P4	2.042369	1.15×10 ⁻²³	2.76×10 ⁻²²
ARHGEF19	2.033833	1.69×10 ⁻²³	3.97×10 ⁻²²
BRCA1	2.03355	1.00×10 ⁻²⁸	3.91×10 ⁻²⁷
PSRC1	2.024931	1.76×10 ⁻²⁸	6.72×10 ⁻²⁷
NPM3	2.000481	1.07×10 ⁻²⁶	3.46×10 ⁻²⁵
C19orf48	1.996467	1.51×10 ⁻³³	8.91×10 ⁻³²
PAICS	1.996222	8.92×10 ⁻³⁶	6.32×10 ⁻³⁴
CKAP2	1.992419	4.21×10 ⁻³⁷	3.29×10 ⁻³⁵
ZNF367	1.984007	1.55×10 ⁻²³	3.68×10 ⁻²²
SC65	1.975876	2.87×10 ⁻²⁴	7.39×10 ⁻²³
NME1	1.975238	6.32×10 ⁻³⁰	2.71×10 ⁻²⁸
SFXN1	1.966853	2.33×10 ⁻³²	1.24×10 ⁻³⁰
GEN1	1.965931	2.50×10 ⁻³¹	1.19×10 ⁻²⁹
FBXO45	1.965829	8.91×10 ⁻²⁹	3.51×10 ⁻²⁷
LMNB2	1.952732	4.63×10 ⁻²⁷	1.56×10 ⁻²⁵
CENPL	1.944313	7.20×10 ⁻³²	3.63×10 ⁻³⁰
TTLL12	1.940079	2.19×10 ⁻²³	5.08×10 ⁻²²
FKBP4	1.935821	7.48×10 ⁻²⁹	2.97×10 ⁻²⁷
FIGNL1	1.934356	3.44×10 ⁻²⁹	1.40×10 ⁻²⁷
SNHG1	1.921614	7.98×10 ⁻²⁵	2.16×10 ⁻²³
DBF4	1.91524	1.68×10 ⁻²⁹	6.95×10 ⁻²⁸
SHMT2	1.908972	2.72×10 ⁻³⁷	2.14×10 ⁻³⁵
ZC3H8	1.900819	2.01×10 ⁻³⁵	1.37×10 ⁻³³
FAM162A	1.890852	3.60×10 ⁻²⁴	9.17×10 ⁻²³
GINS3	1.889239	7.18×10 ⁻²⁹	2.85×10 ⁻²⁷
C15orf23	1.885699	2.53×10 ⁻³⁶	1.87×10 ⁻³⁴

Gene symbol	Log ₂ FC	p-value	FDR
ZWILCH	1.871181	1.53×10 ⁻⁴²	1.69×10 ⁻⁴⁰
E2F1	1.860271	8.73×10 ⁻²³	1.91×10 ⁻²¹
TFAP4	1.860016	3.53×10 ⁻³²	1.84×10 ⁻³⁰
ALG3	1.858391	1.29×10 ⁻²⁴	3.44×10 ⁻²³
GMPS	1.857272	1×10×10 ⁻³⁰	5.01×10 ⁻²⁹
CENPN	1.849211	2.53×10 ⁻³²	1.34×10 ⁻³⁰
CCDC58	1.84462	1.27×10 ⁻²⁸	4.93×10 ⁻²⁷
EPT1	1.842269	1.74×10 ⁻²⁴	4.56×10 ⁻²³
FANCE	1.839178	5.42×10 ⁻²⁵	1.49×10 ⁻²³
C21orf45	1.824319	7.93×10 ⁻³²	3.96×10 ⁻³⁰
H2AFX	1.817084	9.01×10 ⁻²⁷	2.94×10 ⁻²⁵
CENPO	1.805156	8.70×10 ⁻³⁶	6.18×10 ⁻³⁴
SIAH2	1.800595	5.96×10 ⁻²³	1.32×10 ⁻²¹
NUP155	1.799484	1.07×10 ⁻²⁶	3.46×10 ⁻²⁵
TUBA1C	1.794549	7.15×10 ⁻³²	3.62×10 ⁻³⁰
SASS6	1.794024	2.06×10 ⁻³³	1.21×10 ⁻³¹
DONSON	1.793253	5.06×10 ⁻³¹	2.36×10 ⁻²⁹
POLR2H	1.781748	1.88×10 ⁻²⁷	6.54×10 ⁻²⁶
PCNA	1.781456	3.59×10 ⁻³⁴	2.20×10 ⁻³²
TCF19	1.777564	1.43×10 ⁻³⁰	6.47×10 ⁻²⁹
NUDT1	1.776414	8.38×10 ⁻²⁶	2.52×10 ⁻²⁴
RPP40	1.772523	7.85×10 ⁻²⁹	3×10×10 ⁻²⁷
TACC3	1.767938	5.36×10 ⁻²⁷	1.79×10 ⁻²⁵
EFNA4	1.765292	1.40×10 ⁻²⁶	4.45×10 ⁻²⁵
C6orf167	1.763462	3.96×10 ⁻²⁸	1.46×10 ⁻²⁶
INCENP	1.754252	2.62×10 ⁻²⁷	9.02×10 ⁻²⁶
MYO19	1.746419	1.81×10 ⁻³⁰	8.09×10 ⁻²⁹
POC1A	1.741735	9.78×10 ⁻³⁰	4.13×10 ⁻²⁸
MCM6	1.740524	1.47×10 ⁻³¹	7×10×10 ⁻³⁰
PPP1R14B	1.739573	8.85×10 ⁻²⁷	2.89×10 ⁻²⁵
PSMC3IP	1.735825	2.85×10 ⁻²³	6.52×10 ⁻²²
RFC5	1.734643	2.79×10 ⁻³²	1.47×10 ⁻³⁰
C15orf41	1.732808	3.43×10 ⁻²⁵	9.67×10 ⁻²⁴
GGCT	1.729941	2.79×10 ⁻³¹	1.33×10 ⁻²⁹
C20orf72	1.727364	7.35×10 ⁻³⁶	5.26×10 ⁻³⁴
YDJC	1.724798	3.80×10 ⁻²³	8.62×10 ⁻²²
RCCD1	1.706089	6.60×10 ⁻²⁷	2.19×10 ⁻²⁵
BRI3BP	1.700324	1.04×10 ⁻²⁵	3.11×10 ⁻²⁴
BRIX1	1.696138	9.09×10 ⁻²⁷	2.96×10 ⁻²⁵
PPIF	1.694674	1.49×10 ⁻²⁵	4.41×10 ⁻²⁴
GRHL2	1.686725	1.60×10 ⁻²⁴	4.23×10 ⁻²³
PUS7	1.670735	9.94×10 ⁻²⁷	3.23×10 ⁻²⁵
ESRP1	1.666918	1.93×10 ⁻³⁰	8.64×10 ⁻²⁹

Gene symbol	Log ₂ FC	p-value	FDR
CCT5	1.655027	1.25×10 ⁻²⁹	5.23×10 ⁻²⁸
RANBP1	1.650848	6.50×10 ⁻²⁸	2.34×10 ⁻²⁶
DKC1	1.635363	6.84×10 ⁻³²	3.47×10 ⁻³⁰
SUV39H2	1.628626	5.34×10 ⁻²⁷	1.79×10 ⁻²⁵
KIF20B	1.627967	2.02×10 ⁻²³	4.72×10 ⁻²²
XPOT	1.623617	2.56×10 ⁻²⁶	7.94×10 ⁻²⁵
C3orf26	1.612231	6.70×10 ⁻²⁴	1.67×10 ⁻²²
COQ3	1.602896	1.08×10 ⁻²⁵	3.21×10 ⁻²⁴
UNG	1.596097	2.84×10 ⁻³²	1.49×10 ⁻³⁰
RCC2	1.589286	1.36×10 ⁻³⁰	6.16×10 ⁻²⁹
RSRC1	1.582151	1.70×10 ⁻²⁵	5.00×10 ⁻²⁴
TPI1	1.578752	4.03×10 ⁻²⁶	1.24×10 ⁻²⁴
C12orf11	1.569481	7.47×10 ⁻³²	3.76×10 ⁻³⁰
PSMD2	1.563227	3.47×10 ⁻²³	7.89×10 ⁻²²
MRPL47	1.56228	2.12×10 ⁻²²	4.44×10 ⁻²¹
ZFP64	1.559335	4.91×10 ⁻³²	2.54×10 ⁻³⁰
MRPL3	1.555203	8.39×10 ⁻³³	4.62×10 ⁻³¹
DDX39	1.551532	4.41×10 ⁻²²	8.99×10 ⁻²¹
C20orf20	1.549278	4.98×10 ⁻³⁴	3.00×10 ⁻³²
TMEM177	1.546582	5.83×10 ⁻²⁷	1.94×10 ⁻²⁵
TOPBP1	1.542732	1.02×10 ⁻²⁴	2.73×10 ⁻²³
RUVBL1	1.538438	4.95×10 ⁻²⁹	1.99×10 ⁻²⁷
HPRT1	1.536165	9.56×10 ⁻²⁴	2.32×10 ⁻²²
MCM5	1.523754	4.06×10 ⁻²³	9.17×10 ⁻²²
DTYMK	1.518073	4.07×10 ⁻²³	9.19×10 ⁻²²
WDR12	1.511362	2.90×10 ⁻²⁸	1.09×10 ⁻²⁶
NIPSNAP1	1.503167	8.94×10 ⁻²⁴	2.18×10 ⁻²²
CCDC99	1.500315	5.71×10 ⁻²⁸	2.07×10 ⁻²⁶
PSMG3	1.500262	4.33×10 ⁻²⁴	1×10 ⁻²²
RRM1	1.498123	2.26×10 ⁻²²	4.72×10 ⁻²¹
PRIM2	1.497858	1.66×10 ⁻²⁴	4.36×10 ⁻²³
DNAJB11	1.489187	8.45×10 ⁻²³	1.85×10 ⁻²¹
SSX2IP	1.478768	1.76×10 ⁻²²	3.71×10 ⁻²¹
WDR53	1.475187	4.87×10 ⁻²³	1.09×10 ⁻²¹
CCDC21	1.472295	2.22×10 ⁻²²	4.64×10 ⁻²¹
SNRPA1	1.469414	1.61×10 ⁻³²	8.62×10 ⁻³¹
CSE1L	1.461911	4.29×10 ⁻³⁷	3.34×10 ⁻³⁵
TARS	1.459509	2.12×10 ⁻²⁵	6.13×10 ⁻²⁴
WDR67	1.45802	3.74×10 ⁻²⁵	1.05×10 ⁻²³
TIMM8A	1.457409	1.87×10 ⁻²²	3.94×10 ⁻²¹
RAE1	1.457224	6.13×10 ⁻³⁶	4.43×10 ⁻³⁴
KIF22	1.450715	1.56×10 ⁻²⁴	4.13×10 ⁻²³
C10orf2	1.438043	9.56×10 ⁻²⁴	2.32×10 ⁻²²

Gene symbol	Log ₂ FC	p-value	FDR
RFWD3	1.43459	2.11×10 ⁻²⁸	8.00×10 ⁻²⁷
DCUN1D5	1.427376	9.02×10 ⁻²³	1.96×10 ⁻²¹
CPOX	1.424399	2.66×10 ⁻²⁴	6.87×10 ⁻²³
SRPK1	1.420745	5.62×10 ⁻³¹	2.61×10 ⁻²⁹
TMEM48	1.420536	5.64×10 ⁻²⁴	1.41×10 ⁻²²
DCAF13	1.418586	3.15×10 ⁻³¹	1.50×10 ⁻²⁹
HSPD1	1.416285	1.47×10 ⁻²⁴	3.90×10 ⁻²³
C16orf88	1.403693	3.89×10 ⁻²⁷	1.32×10 ⁻²⁵
TMEM189	1.395716	4.22×10 ⁻²³	9.51×10 ⁻²²
C12orf32	1.387765	3.33×10 ⁻²³	7.59×10 ⁻²²
FLAD1	1.382984	1.05×10 ⁻³²	5.74×10 ⁻³¹
DUS4L	1.382626	2.15×10 ⁻²⁴	5.59×10 ⁻²³
RANGAP1	1.373125	9.71×10 ⁻²⁴	2.35×10 ⁻²²
BYSL	1.369132	1.61×10 ⁻²⁴	4.23×10 ⁻²³
CSTF2	1.368053	3.96×10 ⁻²³	8.96×10 ⁻²²
CCDC86	1.348674	2.35×10 ⁻²⁵	6.77×10 ⁻²⁴
XPO5	1.344048	8.53×10 ⁻²⁵	2.31×10 ⁻²³
DNAJC9	1.34322	3.94×10 ⁻³⁰	1.72×10 ⁻²⁸
NUP37	1.335745	3.54×10 ⁻²⁵	9.96×10 ⁻²⁴
SPATS2	1.333956	1.20×10 ⁻³¹	5.89×10 ⁻³⁰
PRMT3	1.333228	9.79×10 ⁻²³	2.13×10 ⁻²¹
C1orf131	1.330127	1.36×10 ⁻²⁴	3.61×10 ⁻²³
DSN1	1.329328	4.50×10 ⁻²²	9.16×10 ⁻²¹
B4GALT2	1.322937	9.35×10 ⁻²⁵	2.52×10 ⁻²³
NAA50	1.310484	4.29×10 ⁻²⁵	1.20×10 ⁻²³
TBRG4	1.308868	1.24×10 ⁻²⁶	3.99×10 ⁻²⁵
CDK4	1.305936	3.04×10 ⁻²⁴	7.81×10 ⁻²³
PGAM5	1.2979	2.13×10 ⁻²²	4.45×10 ⁻²¹
CCT3	1.296152	3.16×10 ⁻³³	1.83×10 ⁻³¹
NOP56	1.283091	1.02×10 ⁻²³	2.47×10 ⁻²²
METAP1	1.272501	1.05×10 ⁻²²	2.28×10 ⁻²¹
SNRPD1	1.271744	1.27×10 ⁻²²	2.72×10 ⁻²¹
YWHAZ	1.253088	2.60×10 ⁻²⁵	7.46×10 ⁻²⁴
WDR75	1.248956	2.31×10 ⁻³¹	1.11×10 ⁻²⁹
OLA1	1.247661	1.13×10 ⁻²²	2.44×10 ⁻²¹
TUBG1	1.241358	2.71×10 ⁻²⁵	7.74×10 ⁻²⁴
RFC2	1.23377	2.51×10 ⁻²³	5.78×10 ⁻²²
B3GALNT2	1.232065	1.80×10 ⁻²⁴	4.71×10 ⁻²³
TH1L	1.228534	4.96×10 ⁻²⁴	1.25×10 ⁻²²
ALDH18A1	1.227343	4.89×10 ⁻³¹	2.29×10 ⁻²⁹
FAM136A	1.225345	6.55×10 ⁻²⁴	1.63×10 ⁻²²
MEMO1	1.221739	1.50×10 ⁻²²	3.19×10 ⁻²¹
TFB2M	1.217213	6.72×10 ⁻²³	1.49×10 ⁻²¹

Gene symbol	Log ₂ FC	p-value	FDR
MTIF2	1.213798	1.33×10 ⁻²⁶	4.27×10 ⁻²⁵
TUBB	1.203806	2.31×10 ⁻²³	5.33×10 ⁻²²
FAM189B	1.197619	5.38×10 ⁻²³	1.20×10 ⁻²¹
HN1L	1.193616	4.83×10 ⁻²⁴	1.22×10 ⁻²²
TRAP1	1.190945	3.01×10 ⁻²²	6.18×10 ⁻²¹
HDGF	1.188787	2.04×10 ⁻²⁷	7.09×10 ⁻²⁶
R3HDM1	1.17991	6.86×10 ⁻²⁴	1.70×10 ⁻²²
HDAC2	1.162676	2.45×10 ⁻²³	5.65×10 ⁻²²
XPO1	1.161185	2.32×10 ⁻²³	5.35×10 ⁻²²
SLC25A39	1.140258	2.78×10 ⁻²²	5.75×10 ⁻²¹
CSNK2A1	1.133161	1.57×10 ⁻²²	3.34×10 ⁻²¹
HDAC1	1.129796	6.97×10 ⁻²⁴	1.72×10 ⁻²²
INTS8	1.129134	7×10 ⁻²⁴	1.75×10 ⁻²²
FARSB	1.118461	3×10 ⁻²⁴	7.95×10 ⁻²³
TMEM69	1.115962	3.67×10 ⁻²⁶	1.13×10 ⁻²⁴
TRAF7	1.10877	7.67×10 ⁻²³	1.69×10 ⁻²¹
NOL10	1.077903	8.73×10 ⁻²⁶	2.62×10 ⁻²⁴
PALB2	1.061808	1.82×10 ⁻²³	4.27×10 ⁻²²
CPSF3	1.05951	5.15×10 ⁻²³	1.15×10 ⁻²¹
DENR	1.056722	1.01×10 ⁻³¹	5.04×10 ⁻³⁰
PRPF19	1.045652	3.00×10 ⁻²⁹	1.23×10 ⁻²⁷
PSMD12	1.035537	4.44×10 ⁻²²	9.04×10 ⁻²¹
PPM1G	0.988628	1.01×10 ⁻²³	2.45×10 ⁻²²
TAF2	0.986898	1.37×10 ⁻²³	3.26×10 ⁻²²
CCT7	0.976101	1.48×10 ⁻²²	3.15×10 ⁻²¹
KCMF1	0.937533	2.22×10 ⁻²⁴	5.76×10 ⁻²³
Down-regulation			
LOC149620	-12.1594	2.40×10 ⁻²⁷	8.31×10 ⁻²⁶
CYP1A2	-9.76271	1.98×10 ⁻²³	4.63×10 ⁻²²
CAV3	-9.34724	3.51×10 ⁻²⁶	1.08×10 ⁻²⁴
OTC	-9.08217	1.61×10 ⁻²²	3.42×10 ⁻²¹
CLDN18	-8.69477	5.95×10 ⁻²⁸	2.15×10 ⁻²⁶
LOC572558	-8.66928	1.46×10 ⁻²⁶	4.65×10 ⁻²⁵
LCN6	-8.61148	8.39×10 ⁻²³	1.84×10 ⁻²¹
GUCA2A	-8.36433	4.32×10 ⁻²³	9.72×10 ⁻²²
GP9	-8.36052	4.11×10 ⁻²²	8.40×10 ⁻²¹
OR6K3	-8.17655	2.75×10 ⁻²⁹	1.13×10 ⁻²⁷
CELA2B	-7.98306	7.15×10 ⁻²⁷	2.36×10 ⁻²⁵
HBM	-7.84657	1.22×10 ⁻³¹	5.96×10 ⁻³⁰
AGER	-7.5324	3.96×10 ⁻⁴⁶	5.57×10 ⁻⁴⁴
RXFP2	-7.28848	4.61×10 ⁻³⁸	3.85×10 ⁻³⁶
ACSM2A	-7.19524	1.04×10 ⁻²⁴	2.78×10 ⁻²³
GGTLC1	-7.10107	4.79×10 ⁻²⁷	1.62×10 ⁻²⁵

Gene symbol	Log ₂ FC	p-value	FDR
CLEC1B	-6.89042	1.58×10 ⁻²⁶	5.01×10 ⁻²⁵
TNNC1	-6.81653	5.85×10 ⁻²⁸	2.12×10 ⁻²⁶
MS4A15	-6.81476	2.34×10 ⁻²²	4.87×10 ⁻²¹
CELA2A	-6.6855	1.73×10 ⁻²⁵	5.07×10 ⁻²⁴
C19orf59	-6.5794	1.43×10 ⁻⁴¹	1.48×10 ⁻³⁹
GPIHBP1	-6.52689	7.73×10 ⁻³²	3.87×10 ⁻³⁰
ADAMTS8	-6.45812	9.52×10 ⁻²⁹	3.73×10 ⁻²⁷
GPD1	-6.27275	6×10 ⁻⁴⁹	1.00×10 ⁻⁴⁶
CLIC5	-6.11393	1.90×10 ⁻⁴¹	1.92×10 ⁻³⁹
FIGF	-6.07733	2.45×10 ⁻²⁸	9.23×10 ⁻²⁷
FAM107A	-6.03707	4.42×10 ⁻⁴²	4.70×10 ⁻⁴⁰
HBB	-5.97249	1.31×10 ⁻²⁵	3.89×10 ⁻²⁴
SCUBE1	-5.93284	1.11×10 ⁻²²	2.39×10 ⁻²¹
TMEM100	-5.91513	3.29×10 ⁻³¹	1.56×10 ⁻²⁹
CACNA2D2	-5.84434	5.15×10 ⁻³⁵	3.40×10 ⁻³³
PRG4	-5.75692	2.24×10 ⁻²⁸	8.45×10 ⁻²⁷
FCN3	-5.65536	6.26×10 ⁻³⁶	4.51×10 ⁻³⁴
VEPH1	-5.64109	1.67×10 ⁻²⁷	5.82×10 ⁻²⁶
INMT	-5.63399	1.16×10 ⁻⁴³	1.34×10 ⁻⁴¹
MARCO	-5.52177	1.72×10 ⁻²⁵	5.03×10 ⁻²⁴
HBA2	-5.47844	6.69×10 ⁻³³	3.72×10 ⁻³¹
DES	-5.46299	1.94×10 ⁻²⁴	5.06×10 ⁻²³
SUSD2	-5.43893	2.00×10 ⁻³⁷	1.60×10 ⁻³⁵
TNXB	-5.41186	2.72×10 ⁻³⁷	2.14×10 ⁻³⁵
C4orf31	-5.3604	1.31×10 ⁻²⁶	4.21×10 ⁻²⁵
CLEC3B	-5.2613	1.67×10 ⁻⁴⁹	2.85×10 ⁻⁴⁷
TCF21	-5.23207	1.65×10 ⁻³⁹	1.56×10 ⁻³⁷
ACOXL	-5.22572	1.96×10 ⁻²⁹	8.11×10 ⁻²⁸
LRRC36	-5.22474	1.50×10 ⁻³²	8×10 ⁻³¹
SLC46A2	-5.0746	1.07×10 ⁻³²	5.82×10 ⁻³¹
FAM189A2	-5.04331	4.41×10 ⁻²⁴	1.11×10 ⁻²²
CCL14	-4.99403	1.72×10 ⁻²³	4.05×10 ⁻²²
COL4A3	-4.97118	1.35×10 ⁻²³	3.23×10 ⁻²²
FHL5	-4.93128	5.90×10 ⁻³²	3.02×10 ⁻³⁰
GPR133	-4.88507	6.57×10 ⁻³²	3.34×10 ⁻³⁰
IL1RL1	-4.85547	1.41×10 ⁻²³	3.35×10 ⁻²²
ABCA3	-4.8312	2.03×10 ⁻²³	4.73×10 ⁻²²
GYPB	-4.80865	1.45×10 ⁻³²	7.90×10 ⁻³¹
ATOH8	-4.77835	3.88×10 ⁻³⁰	1.69×10 ⁻²⁸
LRRK2	-4.72852	1.71×10 ⁻²⁶	5.40×10 ⁻²⁵
GCOM1	-4.72595	2.22×10 ⁻³³	1.30×10 ⁻³¹
LPL	-4.6552	1.04×10 ⁻³¹	5.14×10 ⁻³⁰
PREX2	-4.59971	2.77×10 ⁻²²	5.72×10 ⁻²¹

Gene symbol	Log ₂ FC	p-value	FDR
MRC1	-4.59473	1.05×10 ⁻²⁹	4.43×10 ⁻²⁸
FOSB	-4.58346	1.56×10 ⁻²³	3.70×10 ⁻²²
C1QTNF7	-4.57173	2.80×10 ⁻²³	6.40×10 ⁻²²
PDK4	-4.51265	1.00×10 ⁻²⁶	3.25×10 ⁻²⁵
LYVE1	-4.49784	2.27×10 ⁻³⁶	1.69×10 ⁻³⁴
EDNRB	-4.48935	2.39×10 ⁻³⁸	2.04×10 ⁻³⁶
NPR1	-4.4785	1.11×10 ⁻³⁸	9.80×10 ⁻³⁷
PGM5	-4.47487	3.50×10 ⁻²⁴	8.94×10 ⁻²³
HSD17B6	-4.46056	9.00×10 ⁻⁴⁹	1.45×10 ⁻⁴⁶
CCDC48	-4.42839	2.32×10 ⁻³⁹	2.19×10 ⁻³⁷
PLAC9	-4.42012	1.55×10 ⁻²⁵	4.57×10 ⁻²⁴
LRRN3	-4.4158	9.76×10 ⁻²⁴	2.36×10 ⁻²²
AFF3	-4.39441	2.44×10 ⁻²⁷	8.42×10 ⁻²⁶
TEK	-4.37102	1.40×10 ⁻⁴³	1.61×10 ⁻⁴¹
HIGD1B	-4.36867	1.48×10 ⁻³²	8.01×10 ⁻³¹
NOSTRIN	-4.36725	4.05×10 ⁻⁴⁴	5.04×10 ⁻⁴²
FHL1	-4.33598	2.35×10 ⁻³⁹	2.21×10 ⁻³⁷
STEAP4	-4.33369	1.27×10 ⁻²²	2.72×10 ⁻²¹
GPR116	-4.30121	1.71×10 ⁻⁴⁵	2.31×10 ⁻⁴³
SELENBP1	-4.28763	1.64×10 ⁻²⁸	6.26×10 ⁻²⁷
SYT15	-4.28341	5.03×10 ⁻³³	2.85×10 ⁻³¹
SLC19A3	-4.26624	1.13×10 ⁻²³	2.72×10 ⁻²²
SDPR	-4.23925	6.95×10 ⁻²⁸	2.49×10 ⁻²⁶
DLC1	-4.22143	1.08×10 ⁻⁴³	1.27×10 ⁻⁴¹
HSPB6	-4.21033	5.11×10 ⁻³³	2.89×10 ⁻³¹
AQP1	-4.19197	8.63×10 ⁻³⁵	5.59×10 ⁻³³
SLC39A8	-4.19155	5.97×10 ⁻⁴⁴	7.29×10 ⁻⁴²
MFAP4	-4.16775	2.56×10 ⁻²⁵	7.39×10 ⁻²⁴
ABI3BP	-4.14267	9.53×10 ⁻²⁵	2.56×10 ⁻²³
OLR1	-4.14203	3.94×10 ⁻²⁵	1×10 ⁻²³
KL	-4.12562	6.31×10 ⁻²⁵	1.73×10 ⁻²³
EMCN	-4.08201	1.45×10 ⁻³⁵	1.00×10 ⁻³³
CPAMD8	-4.06285	4.48×10 ⁻²⁵	1.25×10 ⁻²³
MMRN1	-4.05246	8.48×10 ⁻²³	1.86×10 ⁻²¹
RTKN2	-4.04405	5.50×10 ⁻⁴⁶	7.68×10 ⁻⁴⁴
FMO2	-4.02069	8.74×10 ⁻²⁵	2.36×10 ⁻²³
AOC3	-4.01357	1.26×10 ⁻³³	7.48×10 ⁻³²
SHE	-4.00092	1.66×10 ⁻³⁶	1.25×10 ⁻³⁴
C11orf9	-4.0003	2.69×10 ⁻²³	6.17×10 ⁻²²
FBP1	-3.99803	3.06×10 ⁻²⁹	1.25×10 ⁻²⁷
ARC	-3.99555	5.07×10 ⁻²⁵	1.40×10 ⁻²³
WISP2	-3.98576	7.95×10 ⁻²³	1.75×10 ⁻²¹
ABCC6	-3.94026	1.17×10 ⁻³⁰	5.33×10 ⁻²⁹

Gene symbol	Log ₂ FC	p-value	FDR
C6orf174	-3.88844	5.79×10 ⁻²⁶	1.76×10 ⁻²⁴
ROBO4	-3.87091	6.42×10 ⁻⁵⁰	1.12×10 ⁻⁴⁷
FMO5	-3.8698	2.25×10 ⁻²⁶	7.02×10 ⁻²⁵
VSIG4	-3.86189	6.51×10 ⁻²⁵	1.77×10 ⁻²³
A2M	-3.85029	4.70×10 ⁻³⁶	3.43×10 ⁻³⁴
SPOCK2	-3.84969	5.18×10 ⁻²⁹	2.08×10 ⁻²⁷
CCDC85A	-3.84811	3.00×10 ⁻²⁸	1.12×10 ⁻²⁶
GPX3	-3.79982	7.52×10 ⁻³²	3.77×10 ⁻³⁰
ARHGAP6	-3.79806	3.67×10 ⁻³¹	1.73×10 ⁻²⁹
PRX	-3.79235	4.63×10 ⁻³⁹	4.24×10 ⁻³⁷
USHBP1	-3.78211	8.39×10 ⁻³⁹	7.52×10 ⁻³⁷
SLC1A1	-3.77875	1.58×10 ⁻³²	8.50×10 ⁻³¹
CD36	-3.76877	8.32×10 ⁻²³	1.83×10 ⁻²¹
PTPRB	-3.75289	4.22×10 ⁻⁴⁴	5.18×10 ⁻⁴²
SIPR1	-3.74494	3.83×10 ⁻⁴⁰	3.71×10 ⁻³⁸
SPN	-3.73016	2.72×10 ⁻²⁹	1.12×10 ⁻²⁷
LIMCH1	-3.72854	4.65×10 ⁻²⁸	1.70×10 ⁻²⁶
AKAP2	-3.71963	1.75×10 ⁻³⁰	7.87×10 ⁻²⁹
FGFR4	-3.71134	1.39×10 ⁻²⁶	4.44×10 ⁻²⁵
TAL1	-3.71046	2.97×10 ⁻³¹	1.41×10 ⁻²⁹
ALDH3B1	-3.69884	5.40×10 ⁻³²	2.79×10 ⁻³⁰
KANK3	-3.69294	4.49×10 ⁻⁴⁹	7.43×10 ⁻⁴⁷
COX4I2	-3.67538	6.99×10 ⁻³⁰	2.99×10 ⁻²⁸
CDH5	-3.67113	1.26×10 ⁻⁴⁴	1.61×10 ⁻⁴²
CLDN5	-3.66702	1.01×10 ⁻³⁰	4.65×10 ⁻²⁹
NRGN	-3.66558	2.83×10 ⁻²⁵	8.05×10 ⁻²⁴
MSR1	-3.6607	8.39×10 ⁻²⁴	2.05×10 ⁻²²
DPEP2	-3.64229	4.71×10 ⁻³⁰	2.04×10 ⁻²⁸
CX3CR1	-3.62554	1.22×10 ⁻²³	2.92×10 ⁻²²
LOC158376	-3.62252	3.99×10 ⁻³¹	1.88×10 ⁻²⁹
ARHGEF15	-3.61949	3.07×10 ⁻⁴⁴	3.89×10 ⁻⁴²
SOX17	-3.61647	3.27×10 ⁻³⁷	2.56×10 ⁻³⁵
ECSCR	-3.60883	2.05×10 ⁻³⁷	1.63×10 ⁻³⁵
RICH2	-3.58888	1.36×10 ⁻²⁸	5.26×10 ⁻²⁷
PRAM1	-3.58695	3.58×10 ⁻²⁸	1.33×10 ⁻²⁶
PTH1R	-3.58311	3.39×10 ⁻²⁵	9.57×10 ⁻²⁴
CD52	-3.58154	1.59×10 ⁻²⁷	5.55×10 ⁻²⁶
C13orf15	-3.56071	1.53×10 ⁻⁴⁹	2.64×10 ⁻⁴⁷
HYAL1	-3.55975	2.04×10 ⁻³⁰	9×10 ⁻²⁹
VIPR1	-3.54455	3.84×10 ⁻²⁷	1.31×10 ⁻²⁵
PKNOX2	-3.54264	7.29×10 ⁻²⁴	1.79×10 ⁻²²
LDB2	-3.52548	5.25×10 ⁻⁴⁵	6.91×10 ⁻⁴³
GLDN	-3.52371	5.12×10 ⁻²⁹	2.06×10 ⁻²⁷

Gene symbol	Log ₂ FC	p-value	FDR
CGNL1	-3.52076	1.23×10 ⁻²⁷	4.35×10 ⁻²⁶
ADRB2	-3.51951	2.03×10 ⁻²³	4.73×10 ⁻²²
F10	-3.50705	1.67×10 ⁻²²	3.53×10 ⁻²¹
JPH4	-3.50174	4.63×10 ⁻²²	9.40×10 ⁻²¹
RASGRP4	-3.49912	4.28×10 ⁻³²	2.23×10 ⁻³⁰
CAV1	-3.48723	6×10 ⁻³¹	2.82×10 ⁻²⁹
HOPX	-3.48553	5.64×10 ⁻²³	1.25×10 ⁻²¹
FAM162B	-3.47565	2.80×10 ⁻³⁰	1.24×10 ⁻²⁸
SEMA3B	-3.4732	1.80×10 ⁻²⁴	4.71×10 ⁻²³
CFP	-3.46713	1.13×10 ⁻²⁹	4.75×10 ⁻²⁸
GIMAP8	-3.46577	1.77×10 ⁻³⁶	1.32×10 ⁻³⁴
PHACTR1	-3.46399	2.75×10 ⁻³⁴	1.72×10 ⁻³²
CFD	-3.43599	5.06×10 ⁻³⁰	2.18×10 ⁻²⁸
RAMP3	-3.43498	1.63×10 ⁻³⁶	1.24×10 ⁻³⁴
GRRP1	-3.42659	8.46×10 ⁻³⁹	7.55×10 ⁻³⁷
C5orf4	-3.41819	4.63×10 ⁻³²	2.40×10 ⁻³⁰
SYNE1	-3.41118	2.24×10 ⁻³⁰	9.97×10 ⁻²⁹
LAMP3	-3.4073	3.70×10 ⁻²⁵	1.04×10 ⁻²³
KLF2	-3.40531	1.46×10 ⁻³⁸	1.28×10 ⁻³⁶
ALOX5AP	-3.40389	1.40×10 ⁻²⁵	4.14×10 ⁻²⁴
VWF	-3.39482	3.82×10 ⁻³³	2.18×10 ⁻³¹
OSCAR	-3.3929	1.17×10 ⁻³⁰	5.32×10 ⁻²⁹
GSTM5	-3.38919	1.05×10 ⁻²⁴	2.80×10 ⁻²³
ACVRL1	-3.37762	1.21×10 ⁻⁴⁵	1.66×10 ⁻⁴³
C1orf116	-3.36689	4.27×10 ⁻²⁶	1.31×10 ⁻²⁴
MYCT1	-3.36508	2.63×10 ⁻⁴¹	2.64×10 ⁻³⁹
MS4A7	-3.36205	2.55×10 ⁻²⁶	7.92×10 ⁻²⁵
ALOX5	-3.35924	2.65×10 ⁻²⁵	7.58×10 ⁻²⁴
ARRB1	-3.35891	3.42×10 ⁻³³	1.97×10 ⁻³¹
ESAM	-3.35409	2.52×10 ⁻⁴⁷	3.83×10 ⁻⁴⁵
NLR4	-3.35065	5.43×10 ⁻³⁸	4.46×10 ⁻³⁶
GNG11	-3.33529	3.12×10 ⁻³⁹	2.89×10 ⁻³⁷
CASS4	-3.32876	1.62×10 ⁻²²	3.44×10 ⁻²¹
EPAS1	-3.31795	1.64×10 ⁻³⁸	1.43×10 ⁻³⁶
CD300C	-3.31717	1.88×10 ⁻²²	3.95×10 ⁻²¹
CD93	-3.29485	8.24×10 ⁻³⁵	5.35×10 ⁻³³
TPPP3	-3.27648	2.40×10 ⁻²²	4.99×10 ⁻²¹
PDE2A	-3.27601	2.88×10 ⁻²⁶	8.89×10 ⁻²⁵
CLEC14A	-3.27085	7.32×10 ⁻⁴³	8.16×10 ⁻⁴¹
RAMP2	-3.25241	3.56×10 ⁻⁴⁷	5.33×10 ⁻⁴⁵
AATK	-3.25141	3.24×10 ⁻³⁰	1.42×10 ⁻²⁸
MUSTN1	-3.24645	1.56×10 ⁻²⁵	4.60×10 ⁻²⁴
JAM2	-3.24344	3.37×10 ⁻³⁰	1.48×10 ⁻²⁸

Gene symbol	Log ₂ FC	p-value	FDR
TMEM88	-3.24122	5.12×10 ⁻³⁵	3.39×10 ⁻³³
STARD8	-3.24031	1.32×10 ⁻³⁴	8.40×10 ⁻³³
RNASE1	-3.23871	6.24×10 ⁻²⁶	1.89×10 ⁻²⁴
C20orf160	-3.22963	1.34×10 ⁻³⁵	9.35×10 ⁻³⁴
CSRNP1	-3.22758	1.07×10 ⁻⁴¹	1.12×10 ⁻³⁹
FILIP1	-3.22751	2.37×10 ⁻²³	5.46×10 ⁻²²
CD300LF	-3.22575	1.40×10 ⁻²²	2.98×10 ⁻²¹
ABCA9	-3.22281	1.08×10 ⁻²²	2.33×10 ⁻²¹
LIMS2	-3.22121	2.16×10 ⁻³¹	1.04×10 ⁻²⁹
FOXF1	-3.21372	3.89×10 ⁻³⁴	2.38×10 ⁻³²
CCRL1	-3.20733	3.47×10 ⁻³⁴	2.14×10 ⁻³²
STX11	-3.20687	1.34×10 ⁻²⁹	5.61×10 ⁻²⁸
HSPA12B	-3.20305	5×10 ⁻³⁸	4.22×10 ⁻³⁶
GRAMD2	-3.19444	8.20×10 ⁻²⁶	2.47×10 ⁻²⁴
FBLN5	-3.182	1.35×10 ⁻²⁸	5.21×10 ⁻²⁷
AMICA1	-3.17974	3.65×10 ⁻²⁴	9.28×10 ⁻²³
SEMA3G	-3.17504	3.27×10 ⁻³¹	1.55×10 ⁻²⁹
GPBAR1	-3.16998	2.00×10 ⁻³¹	9.65×10 ⁻³⁰
SHROOM4	-3.16881	1.96×10 ⁻²⁵	5.69×10 ⁻²⁴
PID1	-3.16799	4.51×10 ⁻²⁵	1.25×10 ⁻²³
NR4A1	-3.16398	4.02×10 ⁻²³	9.08×10 ⁻²²
PECAM1	-3.13741	1.02×10 ⁻⁴⁵	1.41×10 ⁻⁴³
RHOBTB2	-3.13389	8.02×10 ⁻²⁸	2.86×10 ⁻²⁶
TNS1	-3.13202	3.99×10 ⁻³⁴	2.43×10 ⁻³²
SH2D3C	-3.11881	2.42×10 ⁻⁴⁴	3.09×10 ⁻⁴²
WWC2	-3.10011	6.68×10 ⁻³⁶	4.79×10 ⁻³⁴
ADAMTSL4	-3.09954	1×10 ⁻²³	2.64×10 ⁻²²
TIE1	-3.097	4.64×10 ⁻³⁴	2.80×10 ⁻³²
DUSP1	-3.09563	3.34×10 ⁻²⁷	1.15×10 ⁻²⁵
C1orf162	-3.08195	7.24×10 ⁻³⁰	3.08×10 ⁻²⁸
FGD5	-3.0782	6.17×10 ⁻²⁷	2.05×10 ⁻²⁵
GPR146	-3.07741	8.21×10 ⁻⁵¹	1.58×10 ⁻⁴⁸
ADCY4	-3.05492	1.61×10 ⁻³¹	7.78×10 ⁻³⁰
NOVA2	-3.04882	1.61×10 ⁻³²	8.62×10 ⁻³¹
DPYSL2	-3.04532	4.03×10 ⁻³⁵	2.68×10 ⁻³³
PALM2-AKAP2	-3.03489	6.21×10 ⁻³³	3.46×10 ⁻³¹
KIAA1462	-3.03453	8.56×10 ⁻³¹	3.94×10 ⁻²⁹
TGFBR2	-3.03452	1.36×10 ⁻³⁸	1.20×10 ⁻³⁶
ITGA10	-3.01868	8.09×10 ⁻²⁴	1.98×10 ⁻²²
CD302	-3.00702	3.53×10 ⁻⁴⁰	3.44×10 ⁻³⁸
RHOJ	-3.00505	4×10 ⁻³³	2.33×10 ⁻³¹
FAM105A	-3.00365	1.23×10 ⁻²⁹	5.17×10 ⁻²⁸
ARHGAP31	-3	2.13×10 ⁻²⁹	8.78×10 ⁻²⁸

Gene symbol	Log ₂ FC	p-value	FDR
GIMAP6	-2.99933	4.50×10 ⁻²⁶	1.37×10 ⁻²⁴
DOK2	-2.98764	2.90×10 ⁻²⁵	8.22×10 ⁻²⁴
DENND2A	-2.98587	1.33×10 ⁻²⁵	3.95×10 ⁻²⁴
TUBB1	-2.98462	6.32×10 ⁻³⁵	4.13×10 ⁻³³
FAM13C	-2.9724	6.72×10 ⁻²³	1.49×10 ⁻²¹
C20orf202	-2.96704	1.57×10 ⁻²³	3.71×10 ⁻²²
SLC11A1	-2.96521	4.93×10 ⁻²⁷	1.66×10 ⁻²⁵
PCDH12	-2.96104	5.91×10 ⁻³³	3.32×10 ⁻³¹
CELF2	-2.95853	6.41×10 ⁻²⁵	1.75×10 ⁻²³
GATA6	-2.9492	8.57×10 ⁻²⁴	2.09×10 ⁻²²
FRY	-2.94557	6.24×10 ⁻²⁴	1.56×10 ⁻²²
FAM23A	-2.94297	1.91×10 ⁻²²	4.02×10 ⁻²¹
SIRPB1	-2.93761	5.37×10 ⁻²³	1.20×10 ⁻²¹
FGR	-2.92074	1.40×10 ⁻²⁶	4.45×10 ⁻²⁵
CCRL2	-2.91867	1.72×10 ⁻²⁴	4.51×10 ⁻²³
TSPAN12	-2.91288	9.95×10 ⁻²⁴	2.40×10 ⁻²²
LRP2BP	-2.89857	4.30×10 ⁻³⁸	3.62×10 ⁻³⁶
SORBS1	-2.89582	1.00×10 ⁻²⁴	2.69×10 ⁻²³
LMO7	-2.89541	7.26×10 ⁻⁴¹	7.17×10 ⁻³⁹
CXorf36	-2.89129	3.14×10 ⁻³⁴	1.95×10 ⁻³²
GIMAP7	-2.88963	4.23×10 ⁻²⁴	1.07×10 ⁻²²
SOD3	-2.88385	2.37×10 ⁻²²	4.92×10 ⁻²¹
PTPRN2	-2.87659	2.90×10 ⁻²³	6.63×10 ⁻²²
SMAD6	-2.87532	9.07×10 ⁻²⁸	3.22×10 ⁻²⁶
C1QTNF2	-2.87313	8.71×10 ⁻²⁴	2.13×10 ⁻²²
ICAM2	-2.86159	5.21×10 ⁻²⁸	1.89×10 ⁻²⁶
LEPR	-2.86025	4.70×10 ⁻²⁸	1.71×10 ⁻²⁶
GRASP	-2.85483	1.69×10 ⁻²⁴	4.44×10 ⁻²³
RPS6KA2	-2.85267	1.53×10 ⁻²⁹	6.34×10 ⁻²⁸
LOC100302650	-2.84493	7.06×10 ⁻²⁴	1.74×10 ⁻²²
MMRN2	-2.84449	3.59×10 ⁻³³	2.06×10 ⁻³¹
PEAR1	-2.84313	3.78×10 ⁻²⁷	1.29×10 ⁻²⁵
RAI2	-2.82967	5.25×10 ⁻²³	1.17×10 ⁻²¹
DRAM1	-2.82645	1.43×10 ⁻³¹	6.92×10 ⁻³⁰
LRRC32	-2.82262	1.25×10 ⁻²⁷	4.38×10 ⁻²⁶
C5AR1	-2.82213	2.59×10 ⁻²⁵	7.43×10 ⁻²⁴
BCL6B	-2.81241	2.95×10 ⁻³⁴	1.84×10 ⁻³²
GIMAP5	-2.80163	1.61×10 ⁻²²	3.41×10 ⁻²¹
MFSD2A	-2.79867	5.38×10 ⁻²⁵	1.48×10 ⁻²³
MGLL	-2.79541	1.06×10 ⁻²²	2.30×10 ⁻²¹
GLIPIR2	-2.79476	5.14×10 ⁻³³	2.90×10 ⁻³¹
SGMS2	-2.78896	6.74×10 ⁻²⁷	2.23×10 ⁻²⁵
IL3RA	-2.78779	2.77×10 ⁻³⁰	1.23×10 ⁻²⁸

Gene symbol	Log ₂ FC	p-value	FDR
TRPV2	-2.78591	2.16×10 ⁻²⁸	8.16×10 ⁻²⁷
CD34	-2.78122	1.13×10 ⁻³⁴	7.21×10 ⁻³³
ARHGAP29	-2.77841	4.50×10 ⁻²²	9.16×10 ⁻²¹
F8	-2.77365	8.66×10 ⁻³⁹	7.70×10 ⁻³⁷
CYYR1	-2.76986	1.26×10 ⁻²⁸	4.89×10 ⁻²⁷
PTPRM	-2.76679	3.67×10 ⁻²⁷	1.25×10 ⁻²⁵
PDE1B	-2.7619	7.76×10 ⁻²³	1.71×10 ⁻²¹
DAPK2	-2.75568	3.00×10 ⁻²⁵	8.51×10 ⁻²⁴
ACE	-2.75464	4.75×10 ⁻²⁹	1.92×10 ⁻²⁷
EMP2	-2.74511	8.21×10 ⁻³⁵	5.35×10 ⁻³³
KIF17	-2.74177	2.03×10 ⁻²⁶	6.37×10 ⁻²⁵
KDR	-2.73606	1.11×10 ⁻²⁶	3.57×10 ⁻²⁵
CCDC69	-2.73141	7.48×10 ⁻²⁵	2.03×10 ⁻²³
ERG	-2.72745	1.46×10 ⁻³²	7.93×10 ⁻³¹
SPNS2	-2.70412	4.34×10 ⁻²⁴	1×10 ⁻²²
FLVCR2	-2.70055	8.12×10 ⁻²⁴	1.99×10 ⁻²²
P2RY14	-2.6998	6.86×10 ⁻²³	1.51×10 ⁻²¹
AHCYL2	-2.69686	1.81×10 ⁻³⁸	1.57×10 ⁻³⁶
MFNG	-2.68354	9.22×10 ⁻²⁷	3.00×10 ⁻²⁵
PTPN21	-2.68348	5.92×10 ⁻³⁵	3.89×10 ⁻³³
GRK5	-2.68108	1.62×10 ⁻³⁶	1.23×10 ⁻³⁴
NR5A2	-2.66246	7.92×10 ⁻²⁷	2.60×10 ⁻²⁵
STARD13	-2.66146	2.58×10 ⁻²⁵	7.41×10 ⁻²⁴
S100A4	-2.66043	4.73×10 ⁻²⁷	1.60×10 ⁻²⁵
GADD45B	-2.6507	6.50×10 ⁻²⁹	2.59×10 ⁻²⁷
FLI1	-2.649	1.47×10 ⁻²⁶	4.66×10 ⁻²⁵
CD97	-2.64755	9.65×10 ⁻³⁰	4.08×10 ⁻²⁸
TENC1	-2.64161	2.57×10 ⁻³⁷	2.04×10 ⁻³⁵
FLT4	-2.62828	8.35×10 ⁻²⁶	2.52×10 ⁻²⁴
SELPLG	-2.62733	1.54×10 ⁻²²	3.27×10 ⁻²¹
NOTCH4	-2.61965	4.93×10 ⁻²⁹	1.99×10 ⁻²⁷
RASL12	-2.61474	1.82×10 ⁻²⁶	5.72×10 ⁻²⁵
FZD4	-2.61125	7.71×10 ⁻³⁴	4.59×10 ⁻³²
SPI1	-2.61005	3.72×10 ⁻²²	7.63×10 ⁻²¹
CD55	-2.59833	7.24×10 ⁻³⁰	3.08×10 ⁻²⁸
ZFP36	-2.59747	1.90×10 ⁻²³	4.45×10 ⁻²²
DENND3	-2.58669	2.34×10 ⁻²⁷	8.09×10 ⁻²⁶
KANK2	-2.58518	5.25×10 ⁻³⁸	4.33×10 ⁻³⁶
CABLES1	-2.5802	1.06×10 ⁻²²	2.30×10 ⁻²¹
SCARF1	-2.57314	3.55×10 ⁻³⁴	2.18×10 ⁻³²
ENG	-2.55595	2.48×10 ⁻³²	1.32×10 ⁻³⁰
RNASE4	-2.5375	4.20×10 ⁻²⁸	1.54×10 ⁻²⁶
CYBRD1	-2.52939	4.89×10 ⁻²⁷	1.65×10 ⁻²⁵

Gene symbol	Log ₂ FC	p-value	FDR
GMFG	-2.52643	3.54×10 ⁻²²	7.28×10 ⁻²¹
ATP11A	-2.52404	2.30×10 ⁻³²	1.23×10 ⁻³⁰
CITED2	-2.51951	4.01×10 ⁻²⁸	1.48×10 ⁻²⁶
TSPAN4	-2.4885	1.28×10 ⁻²⁵	3.82×10 ⁻²⁴
ZMYND15	-2.48755	9.02×10 ⁻²³	1.96×10 ⁻²¹
TNFSF13	-2.48415	2.62×10 ⁻³⁴	1.64×10 ⁻³²
CALCRL	-2.46726	3.28×10 ⁻²⁴	8.39×10 ⁻²³
GJA4	-2.46404	4.81×10 ⁻²³	1.08×10 ⁻²¹
AK1	-2.45049	1.71×10 ⁻⁴¹	1.76×10 ⁻³⁹
TMEM204	-2.44978	1.01×10 ⁻²⁴	2.70×10 ⁻²³
DOCK4	-2.42247	9.56×10 ⁻²⁹	3.74×10 ⁻²⁷
CYB5A	-2.39784	7.48×10 ⁻²⁷	2.46×10 ⁻²⁵
SLC9A3R2	-2.3576	3.71×10 ⁻³⁰	1.62×10 ⁻²⁸
LMO2	-2.35363	4.94×10 ⁻²³	1×10 ⁻²¹
ACP5	-2.34384	1.18×10 ⁻²²	2.54×10 ⁻²¹
4-Sep	-2.33403	3.49×10 ⁻²³	7.92×10 ⁻²²
ALDH2	-2.33325	1.00×10 ⁻²⁶	3.25×10 ⁻²⁵
TMEM220	-2.3118	4.31×10 ⁻²⁵	1.20×10 ⁻²³
ELTD1	-2.30969	7.03×10 ⁻²⁴	1.73×10 ⁻²²
DISP1	-2.30803	9.17×10 ⁻²⁸	3.25×10 ⁻²⁶
CD101	-2.30461	2.53×10 ⁻²⁴	6.55×10 ⁻²³
SPRY4	-2.2906	1.74×10 ⁻²⁵	5.09×10 ⁻²⁴
RECK	-2.28789	6.98×10 ⁻²⁴	1.73×10 ⁻²²
HECW2	-2.28144	1.90×10 ⁻²⁵	5.54×10 ⁻²⁴
SULT1A1	-2.27885	3.82×10 ⁻²³	8.66×10 ⁻²²
APOLD1	-2.27838	2.83×10 ⁻²⁵	8.05×10 ⁻²⁴
ADARB1	-2.2767	1.07×10 ⁻²³	2.57×10 ⁻²²
SH3BP5	-2.27126	5.27×10 ⁻²⁵	1.45×10 ⁻²³
ACACB	-2.25686	1.59×10 ⁻²³	3.77×10 ⁻²²
KLF9	-2.25592	1.00×10 ⁻²²	2.18×10 ⁻²¹
SNX30	-2.23315	3.35×10 ⁻³⁸	2.83×10 ⁻³⁶
SNX25	-2.23163	7.67×10 ⁻⁴⁴	9.21×10 ⁻⁴²
MITF	-2.22753	6.91×10 ⁻²⁴	1.71×10 ⁻²²
PDLIM2	-2.19974	1.38×10 ⁻³⁰	6.25×10 ⁻²⁹
EXOC3L	-2.19896	1.49×10 ⁻³⁰	6.71×10 ⁻²⁹
DLL4	-2.19865	2.42×10 ⁻²⁴	6.26×10 ⁻²³
LHFP	-2.18796	6.97×10 ⁻²⁷	2.30×10 ⁻²⁵
TNFSF12	-2.18716	5.01×10 ⁻²⁷	1.68×10 ⁻²⁵
AFAP1L1	-2.17587	1.60×10 ⁻²³	3.79×10 ⁻²²
CAT	-2.17456	1.85×10 ⁻³⁵	1.27×10 ⁻³³
KCNAB1	-2.17312	1.26×10 ⁻²²	2.69×10 ⁻²¹
SASH1	-2.16835	2.02×10 ⁻²³	4.72×10 ⁻²²
ARHGAP18	-2.16043	2.44×10 ⁻²⁶	7.57×10 ⁻²⁵

Gene symbol	Log ₂ FC	p-value	FDR
UNC13B	-2.15658	2×10×10 ⁻²⁶	6.60×10 ⁻²⁵
CD83	-2.13621	2.53×10 ⁻²³	5.81×10 ⁻²²
MOSC2	-2.1361	3.39×10 ⁻²⁶	1.04×10 ⁻²⁴
GPD1L	-2.13328	5.33×10 ⁻²⁸	1.93×10 ⁻²⁶
SECISBP2L	-2.12867	1.67×10 ⁻⁴³	1.91×10 ⁻⁴¹
RBMS2	-2.12845	4.40×10 ⁻³⁰	1.91×10 ⁻²⁸
RBPMS	-2.11909	2.70×10 ⁻²³	6.18×10 ⁻²²
PRKCE	-2.11187	4.55×10 ⁻³⁴	2.76×10 ⁻³²
FAM167B	-2.0907	9.79×10 ⁻²⁸	3.46×10 ⁻²⁶
GPR4	-2.08624	2.52×10 ⁻²⁵	7.27×10 ⁻²⁴
KLF6	-2.08031	2.59×10 ⁻²⁴	6.69×10 ⁻²³
UTRN	-2.0692	2.20×10 ⁻²⁶	6.90×10 ⁻²⁵
TPK1	-2.06624	1.39×10 ⁻²²	2.97×10 ⁻²¹
WFS1	-2.06068	2.74×10 ⁻³³	1.60×10 ⁻³¹
TM6SF1	-2.04218	4.99×10 ⁻²⁶	1.52×10 ⁻²⁴
ADPRH	-2.04099	4.49×10 ⁻²³	1.01×10 ⁻²¹
CISH	-2.03988	4×10×10 ⁻²⁵	1.15×10 ⁻²³
SPTBN1	-2.031	3.11×10 ⁻³⁶	2.30×10 ⁻³⁴
ASAH1	-2.02566	5.74×10 ⁻³³	3.23×10 ⁻³¹
MAGI3	-2.02067	8.57×10 ⁻²⁶	2.57×10 ⁻²⁴
EPB41L5	-2.01828	1.89×10 ⁻³⁵	1.29×10 ⁻³³
LRRC70	-2.01053	3.29×10 ⁻²⁴	8.40×10 ⁻²³
CXCL16	-1.98929	5.62×10 ⁻²⁷	1.87×10 ⁻²⁵
SGK269	-1.97312	6.78×10 ⁻²⁷	2.24×10 ⁻²⁵
PHACTR2	-1.95853	1.36×10 ⁻³⁰	6.16×10 ⁻²⁹
HSD17B11	-1.93331	3.97×10 ⁻²⁸	1.46×10 ⁻²⁶
RILP	-1.9155	8.40×10 ⁻²⁷	2.75×10 ⁻²⁵
ITPR1	-1.8969	1.68×10 ⁻²³	3.95×10 ⁻²²
NPC2	-1.89168	1.58×10 ⁻²³	3.73×10 ⁻²²
RAPGEF2	-1.85502	8.16×10 ⁻³⁰	3.46×10 ⁻²⁸
WWC1	-1.83224	6.80×10 ⁻²⁴	1.69×10 ⁻²²
CFL2	-1.82902	8.54×10 ⁻²⁶	2.57×10 ⁻²⁴
CBX7	-1.81688	2.70×10 ⁻²³	6.19×10 ⁻²²
BTBD9	-1.80959	5.96×10 ⁻²⁵	1.63×10 ⁻²³
MBIP	-1.80156	2.08×10 ⁻²⁵	6.04×10 ⁻²⁴
HPCAL1	-1.79601	8.56×10 ⁻²⁸	3.04×10 ⁻²⁶
KAT2B	-1.7958	3.09×10 ⁻²⁵	8.75×10 ⁻²⁴
RASSF3	-1.79396	1.08×10 ⁻²⁴	2.88×10 ⁻²³
FCGRT	-1.79227	1.95×10 ⁻²⁵	5.67×10 ⁻²⁴
IFT57	-1.78087	4.31×10 ⁻²⁷	1.46×10 ⁻²⁵
HYAL2	-1.77969	1.90×10 ⁻⁴¹	1.92×10 ⁻³⁹
LTA4H	-1.77606	4.98×10 ⁻⁴⁰	4.78×10 ⁻³⁸
RAB27A	-1.76135	1.64×10 ⁻²⁴	4.33×10 ⁻²³

Gene symbol	Log ₂ FC	p-value	FDR
LIMD1	-1.75201	9.09×10 ⁻³⁶	6.41×10 ⁻³⁴
ADCY9	-1.73565	3.69×10 ⁻²²	7.56×10 ⁻²¹
ST6GALNAC6	-1.73117	5.05×10 ⁻³⁸	4.20×10 ⁻³⁶
PXMP4	-1.71915	1.71×10 ⁻²²	3.62×10 ⁻²¹
LATS2	-1.71534	1.42×10 ⁻²²	3.04×10 ⁻²¹
SLC27A3	-1.71357	1.64×10 ⁻²⁹	6.79×10 ⁻²⁸
C7orf23	-1.70414	1.95×10 ⁻²⁸	7.40×10 ⁻²⁷
CRY2	-1.70113	1.86×10 ⁻³²	9.96×10 ⁻³¹
CASKIN2	-1.70048	1.08×10 ⁻²³	2.59×10 ⁻²²
UBL3	-1.6965	3.62×10 ⁻²⁹	1.47×10 ⁻²⁷
AKAP13	-1.69473	1.71×10 ⁻²³	4.02×10 ⁻²²
PLEKHO2	-1.69433	3.80×10 ⁻²³	8.63×10 ⁻²²
PNPLA6	-1.6739	8.43×10 ⁻³²	4.20×10 ⁻³⁰
SNRK	-1.65845	1.25×10 ⁻⁴⁵	1.71×10 ⁻⁴³
DOK4	-1.63599	1.49×10 ⁻²³	3.54×10 ⁻²²
RARA	-1.6346	4.72×10 ⁻²⁸	1.72×10 ⁻²⁶
CALCOCO1	-1.63321	3.91×10 ⁻²⁷	1.33×10 ⁻²⁵
PHF17	-1.62738	1.07×10 ⁻²⁵	3.21×10 ⁻²⁴
VAMP2	-1.61336	6.49×10 ⁻³²	3.31×10 ⁻³⁰
C5orf53	-1.60531	6.50×10 ⁻²³	1.44×10 ⁻²¹
ARRB2	-1.58705	3.24×10 ⁻²⁹	1.32×10 ⁻²⁷
C5orf32	-1.58449	9.32×10 ⁻²⁸	3.30×10 ⁻²⁶
ZBTB47	-1.57621	2.28×10 ⁻²²	4.74×10 ⁻²¹
GNAQ	-1.57187	6.00×10 ⁻³²	3.06×10 ⁻³⁰
SIDT2	-1.56552	4.55×10 ⁻²⁶	1.39×10 ⁻²⁴
FYCO1	-1.53567	5.63×10 ⁻²⁴	1.41×10 ⁻²²
SLC35A1	-1.52742	2.71×10 ⁻²⁵	7.74×10 ⁻²⁴
TAPT1	-1.50832	5.45×10 ⁻³²	2.80×10 ⁻³⁰
C1orf198	-1.50273	4.62×10 ⁻³²	2.40×10 ⁻³⁰
KIF1C	-1.49967	3.00×10 ⁻²³	6.85×10 ⁻²²
MAP3K3	-1.49287	1.47×10 ⁻²⁸	5.66×10 ⁻²⁷
SH3D19	-1.48881	1.09×10 ⁻²³	2.61×10 ⁻²²
CARD8	-1.48471	1.78×10 ⁻²²	3.75×10 ⁻²¹
ARHGEF3	-1.48222	4.88×10 ⁻²⁵	1.35×10 ⁻²³
QSOX1	-1.47036	2.94×10 ⁻²²	6.06×10 ⁻²¹
RILPL2	-1.41977	1.58×10 ⁻²⁴	4.17×10 ⁻²³
RAB8B	-1.41917	5.62×10 ⁻²³	1.25×10 ⁻²¹
BTD	-1.41871	2.49×10 ⁻²²	5.16×10 ⁻²¹
C10orf32	-1.41146	8.63×10 ⁻²³	1.89×10 ⁻²¹
PPM1M	-1.40925	1.13×10 ⁻²²	2.43×10 ⁻²¹
HSD17B4	-1.39029	4.87×10 ⁻³⁶	3.53×10 ⁻³⁴
FAM82A2	-1.33097	7.42×10 ⁻³³	4.09×10 ⁻³¹
ZFP106	-1.32914	2.03×10 ⁻²²	4.25×10 ⁻²¹

Gene symbol	Log ₂ FC	p-value	FDR
STX12	-1.31941	4.61×10 ⁻³¹	2.16×10 ⁻²⁹
C12orf49	-1.30011	6.32×10 ⁻²⁹	2.53×10 ⁻²⁷
BMPR2	-1.29816	4.05×10 ⁻²²	8.29×10 ⁻²¹
SERINC1	-1.29046	3.43×10 ⁻³²	1.80×10 ⁻³⁰
GANC	-1.28085	1.48×10 ⁻²²	3.15×10 ⁻²¹
SDCBP	-1.27078	1.95×10 ⁻²²	4×10 ⁻²¹
GNAI2	-1.23495	2.09×10 ⁻²⁶	6.55×10 ⁻²⁵
CD81	-1.21589	6.65×10 ⁻²⁶	2.01×10 ⁻²⁴
INPP5K	-1.14701	2.93×10 ⁻²⁸	1×10 ⁻²⁶
COL4A3BP	-1.14432	1.75×10 ⁻²⁶	5.50×10 ⁻²⁵
SEC22C	-1.13898	1.14×10 ⁻²⁶	3.68×10 ⁻²⁵
SNX2	-1.02367	9.40×10 ⁻²⁵	2.53×10 ⁻²³
SACM1L	-1.00516	4.74×10 ⁻²⁴	1.20×10 ⁻²²
ZFYVE20	-0.93822	7.39×10 ⁻²⁴	1.82×10 ⁻²²
RHOA	-0.93041	5.87×10 ⁻²⁴	1.47×10 ⁻²²
GORASP1	-0.88378	6.42×10 ⁻²⁵	1.75×10 ⁻²³

FC – fold change; FDR – false discovery rate; lung SCC – lung squamous cell carcinoma.

Supplementary Table 2. The top 10 transcription factors regulated DEGs in lung SCC.

TFs	Log ₂ FC	Up/down	Connectivity	Genes
NFIC	-0.9414	Down	83	FGFR4, FCGRT, CHAF1A, HSD17B4, TMEM69, PLK1, ROBO4, CBLC, GPR116, NAA50, ARHGAP6, MCM6, DTYMK, PTPRM, RPS6KA2, CHRNAS, CYR1, WDR62, ASF1B, GNGT1, TFB2M, GSTM5, ANLN, FLAD1, DNAJB11, MUSTN1, C10orf32, LRRC36, ECT2, PPP1R14B, ALDH2, CRY2, ARC, RNASE4, KRT74, FOXE1, BRCA1, SOX17, C5AR1, FKBP4, POC1A, C1orf162, RNASE1, SLC7A5, FAM72A, CBX7, PGM5, PCDH12, SSX2IP, TM6SF1, PALM2-AKAP2, ACOXL, PITX2, PSAT1, FZD4, DSP, UTRN, KIF22, CENPE, TMEM189, FAM72D, TMEM132A, TERT, DLX6, KIF1C, STX12, GORASP1, ATAD5, TK1, LRRK2, GGCT, KIF11, LMNB1, SLC25A10, ZC3H8, TRPV2, POLR2H, CALCRL, MMRN1, CD34, MMP11, CDC25A, RAB8B
BRCA1	2.0335	Up	82	LIMD1, CELF2, ACACB, CD302, DUSP9, PPAP2C, GORASP1, LAMP3, MCM4, GYLTL1B, FLAD1, TNS4, HSD17B4, STRA6, FAM83D, DAPK2, MARCO, EFNA4, PDE1B, PSRC1, COL4A3, ASAH1, TIMM8A, ERCC6L, CBLC, SORBS1, HOPX, CCDC58, CLEC14A, PLEKHO2, BTBD9, PALB2, KIF4A, SSX2IP, SPOCK2, EDNRB, ADAMTSL4, PTH1R, GGCT, UBE2T, HELLS, ABCC6, ADCY9, NEK2, PHACTR1, TPK1, TROAP, ABCA12, TMPRSS11F, CENPK, PRPF19, ATP11A, TOP2A, SNRPA1, SUV39H2, DSP, SACM1L, HDAC2, ELTD1, TPX2, B4GALNT4, TNXB, GCOM1, PID1, HBB, MYO19, AATK, NLRC4, BLM, SH3BP5, GIMAP6, GLIPR2, GNAQ, MELK, MND1, SKA3, ADAMT58, RPS6KA2, CHAF1A, ITGA10, CALCOCO1
NFATC2	-2.5949	Down	75	IGSF9, SH3BP5, KRT16, PTHLH, PTPN21, CARD8, PSMD12, MELK, GPIHBP1, RAD51AP2, DUSP1, TSPAN12, PKMYT1, PSMC3IP, KANK2, ALDH3B1, ARTN, MYO19, NUDT1, PLAC9, HOXD13, FANCI, AKAP13, KIAA1524, KIF20A, DTYMK, DEPDC1B, VEPH1, PDE1B, NMU, MRPL47, STIL, ASPM, UBE2T, FEN1, SASH1, BIRC5, PLEKHO2, LRRN3, DSCC1, PXMP4, CASS4, MMP12, MARCO, E2F1, FAM162B, SULT1A1, PCDH12, FBLN5, TRAF7, PNPLA6, KIAA0101, FILIP1, DOK2, FAM72B, CBLC, B3GNT4, TPBG, WW2, C1orf162, KRT17, KIF18B, RASAL1, C20orf202, PRKCE, CCNB2, ABCA9, ADAMT58, GAL, LAMP3, RHOA, ADARB1, SCUBE1, NCAPG, TCF19

NR4A2	-2.4142	Down	64	NOVA2, FAM105A, PTPRB, SASS6, GPR4, ARHGAP29, RSRC1, DQX1, SCUBE1, MRPL47, ALDH3B1, PDE2A, POLQ, ALDH2, APOBEC3B, SLC46A2, FRY, E2F2, PITX2, GINS3, C10orf2, CENPL, RAI2, ACP5, CDC25C, SSX2IP, NCAPG2, ATAD2, YWHAZ, E2F7, IRF6, SRD5A1, MCM2, DENND3, NAA50, POC1A, EDNRB, TFAP2A, CDCA8, CCNB2, B3GALNT2, KIF11, CBLC, TMEM100, GIMAP8, CDC25A, COX4I2, CDH5, MELK, FAM131C, TMPRSS11F, PREX2, TPK1, PLEKHG6, GPR87, CSTF2, UHRF1, KIAA1462, KANK3, ADPRH, PGM5, MCM6, CCDC69, MITF
EGR1	-2.1270	Down	45	CLEC3B, SHOX2, EPB41L5, C1QTNF7, PRIM2, SUV39H2, RSRC1, VEPH1, HYAL2, TRIM29, ACACB, TPBG, TMEM79, DOK2, PTPRM, GUCA1A, CX3CR1, SPOCK2, BCL6B, CDCA5, FAM83B, CABLES1, FANCI, TNXB, RIMS2, GRHL1, GPR133, DLL4, WWC1, ENG, UHRF1, ABI3BP, UTRN, PNPLA6, SNRK, ST6GALNAC6, SEMA3B, MEX3A, PDE2A, FAM13C, RASL12, SLC2A1, TMEM132A, ATP11A, WFS1
ELF5	-2.5991	Down	43	ESPL1, RBPMS, GABRA3, DEPDC1B, C1orf112, GJB3, VIPR1, RAB27A, UBL3, FBXO45, MUSTN1, SH3D19, ZIC5, PALM2-AKAP2, KLF9, LIMD1, NUSAP1, GNAI2, DRAM1, AFAP1L1, BTBD9, SLC16A1, DSC3, NR5A2, RHOJ, SH2D3C, HSPB6, PID1, FLI1, RXFP2, ADCY9, SORBS1, PRKCE, DCAF13, TP63, RHOA, FARSB, CCT3, SYT15, CALCRL, ABI3BP, PRIM2, WDR62
HOXA5	-2.0075	Down	43	CENPF, CACNA2D2, NOL10, CCDC34, MELK, PFAFH1B3, ADCY9, RECK, CENPH, FAM105A, SHROOM4, LEPR, GRK5, UNC13B, SRPK1, HDAC1, SGOL1, MYCT1, MARCO, NPR1, SLC1A1, EPAS1, MITF, C12orf49, CYR1, ATAD2, CCDC58, FANCD2, GPD1L, MCM8, DENND3, ESRP1, MTL5, LMNB2, RRM2, SCUBE1, HOXA10, S1PR1, LTA4H, CDC45, HDAC2, RAB27A, AFAP1L1
FOXD1	3.7626	Up	42	SGOL1, TNFSF12, MS4A15, ESCO2, GORASP1, CYB5A, EPAS1, FANCE, GPR116, LRRN3, RAD51AP1, ROBO4, PSMD12, KCNAB1, MTIF2, MBIP, CCDC34, HSD17B11, CABLES1, GRHL2, ELTD1, SHOX2, CAV1, KRTAP4-1, UHRF1, GPRIN1, GPD1L, DSG3, NEK2, YWHAZ, PEAR1, SNX2, COL4A3BP, CDC6, ARHGAP31, CENPO, CLSPN, KIF23, DSC3, SLC7A5, RPS6KA2, ADARB1
ZEB1	-1.8558	Down	40	TNS4, CDC45, NMU, IQGAP3, ACSM2A, TNXB, MYO19, C12orf56, UNG, ARHGAP18, CFD, CENPF, SPTBN2, AATK, CASCS, PECAM1, FLVCR2, NR4A1, SUSD2, PALB2, DNAJB11, FAM83F, TNFSF12, SPATS2, RIMS2, SPNS2, PRAME, TNFSF13, MRPL3, MYCT1, HN1L, RAI2, DCUN1D5, SNX30, KIF15, FGFR4, DTL, FOXE1, MARCO, ANLN
KLF5	1.1064	Up	34	EZH2, MMP11, FLT4, FGR, MFNG, SNX2, JAM2, BOP1, CSRN1, ZWILCH, LMNB2, PXMP4, ESPN, DUSP9, UHRF1, ADAMTSL4, LIMD1, CABLES1, DCAF13, CD97, TRAP1, PRX, UNG, KIF23, CDT1, GPRIN1, GMPS, MAP3K3, RASAL1, FGF11, ARHGAP29, RILPL2, E2F1, TSPAN4

TFs – transcription factors; FC – fold change; lung SCC – lung squamous cell carcinoma.

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