Identification of Key Transcription Factors Associated with Lung Squamous Cell Carcinoma

Feng Zhang  
Xia Chen  
Ke Wei  
Daoming Liu  
Xiaodong Xu  
Xing Zhang  
Hong Shi

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
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 inhibitors [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. Hugl-I functions as a tumor suppressor, and the reduced expression of Hugl-1 shows an inverse correlation with lung SCC progression; inhibition of Hugl-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 included 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.
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.

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 849 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 is 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=2.69×10^{-15}), regulation of multicellular organismal process (GO: 0051239, p=9.39×10^{-10}) and regulation of cell migration (GO: 0030334, p=2.25×10^{-9}) were the most significant enrichments of biological process. Molecular transducer activity (GO: 0004871, p=1.49×10^{-13}), receptor activity (GO: 004872, p=1.67×10^{-12}) and signal transducer activity (GO: 004871, p=1.49×10^{-13}) were the highest for enrichment of molecular function. Membrane part (GO: 0044425, p=3.30×10^{-12}), intrinsic component of membrane (GO: 0031224, p=1.76×10^{-10}), and integral component of membrane (GO: 0016021, p=4.01×10^{-20})
| Gene symbol | Official full name                      | Log_{2} FC | p-value       | FDR       |
|-------------|----------------------------------------|------------|---------------|-----------|
| **Up-regulation (top 15)**                  |            |             |              |           |
| 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^{-24} | 6.57×10^{-23} |
| 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          | 10.7075    | 9.98×10^{-34} | 5.48×10^{-32} |
| GNGT1       | G protein subunit gamma transducin 1    | 10.7104    | 1.29×10^{-25} | 3.82×10^{-23} |
| DLX6        | Distal-less homeobox 6                  | 10.7075    | 1.02×10^{-25} | 6.57×10^{-23} |
| C12orf56    | Chromosome 12 open reading frame 56     | 10.7075    | 1.02×10^{-25} | 6.57×10^{-23} |
| SYT14       | Synaptotagmin 14                        | 10.7075    | 1.02×10^{-25} | 6.57×10^{-23} |
| PITX2       | Paired like homeodomain 2               | 10.7075    | 1.02×10^{-25} | 6.57×10^{-23} |
| DSG3        | Desmoglein 3                            | 10.7075    | 1.02×10^{-25} | 6.57×10^{-23} |
| PGLYRP3     | Peptidoglycan recognition protein 3     | 10.7075    | 1.02×10^{-25} | 6.57×10^{-23} |
| **Down-regulation (top 15)**                |            |             |              |           |
| LOC149620   | Chitinase, acidic pseudogene 2          | -12.1594   | 2.40×10^{-57} | 8.31×10^{-55} |
| 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^{-20} |
| CLDN18      | Claudin 18                              | -8.69477   | 5.95×10^{-28} | 2.15×10^{-26} |
| LOC572558   | PGMS antisense RNA 1                    | -8.66928   | 1.46×10^{-26} | 4.65×10^{-25} |
| LCN6        | Lipocalin 6                             | -8.61418   | 8.39×10^{-23} | 1.84×10^{-21} |
| GUCA2A      | Guanylate cyclase activator 2A          | -8.36431   | 4.32×10^{-21} | 9.72×10^{-20} |
| 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 2B    | -7.98306   | 7.15×10^{-27} | 2.36×10^{-25} |
| HBM         | Hemoglobin subunit mu                   | -7.84657   | 1.22×10^{-21} | 5.96×10^{-20} |
| 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.
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=6.87×10⁻¹⁴), 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.

*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.
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^{-4} |
| GO: 0051239 | Regulation of multicellular organismal process | 9.39×10^{-10} | 2.85×10^{-4} |
| GO: 0030334 | Regulation of cell migration           | 2.25×10^{-9}  | 4.56×10^{-4} |
| GO: 2000145 | Regulation of cell motility            | 2.47×10^{-9}  | 3.75×10^{-4} |
| GO: 0045765 | Regulation of angiogenesis             | 2.67×10^{-9}  | 3.25×10^{-4} |
| GO: 1901342 | Regulation of vasculature development  | 3.89×10^{-9}  | 3.94×10^{-4} |
| GO: 0040012 | Regulation of locomotion               | 4.95×10^{-9}  | 4.30×10^{-4} |
| GO: 0002682 | Regulation of immune system process    | 6.04×10^{-9}  | 4.59×10^{-4} |
| GO: 0051270 | Regulation of cellular component movement | 9.70×10^{-9}  | 6.55×10^{-4} |
| GO: 006897 | Endocytosis                            | 9.86×10^{-9}  | 5.99×10^{-4} |
| GO: 0044765 | Single-organism transport              | 1.04×10^{-8}  | 5.76×10^{-4} |
| GO: 0030155 | Regulation of cell adhesion            | 1.08×10^{-8}  | 5.49×10^{-4} |
| GO: 0048583 | Regulation of response to stimulus     | 1.74×10^{-8}  | 8.16×10^{-4} |
| GO: 0007166 | Cell surface receptor signaling pathway | 2.25×10^{-8}  | 9.75×10^{-4} |
| GO: 0006810 | Transport                              | 2.68×10^{-8}  | 1.09×10^{-4} |
| 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^{-4} |
| GO: 0004871 | Signal transducer activity             | 1.49×10^{-11} | 6.85×10^{-4} |
| GO: 0038023 | Signaling receptor activity            | 1.52×10^{-10} | 5.27×10^{-4} |
| 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^{-4} |
| 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^{-4} |
| GO: 0019825 | Oxygen binding                         | 7.34×10^{-5}  | 7.26×10^{-4} |
| 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       |
|----------|---------------------------------|-----------|-----------|
| GO: 004425 | 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^{-11} |
| GO: 0031226 | Intrinsic component of plasma membrane | 7.88×10^{-15} | 9.90×10^{-12} |
| 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^{-8} |
| GO: 0044333 | Cytoplasmic vesicle part         | 1.18×10^{-7} | 9.92×10^{-4} |
| GO: 0009986 | Cell surface                     | 2.03×10^{-7} | 1.53×10^{-4} |
| GO: 0031090 | Organelle membrane              | 3.75×10^{-7} | 2.57×10^{-4} |
| GO: 0098805 | Whole membrane                   | 4.60×10^{-6} | 2.89×10^{-6} |
| 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 | 22           |
| hsa04115  | p53 signaling pathway             | 2.68E-9    | 1.23E-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.
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, HOX5, 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 carcinogenesis elucidation of lung SCC. 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 in 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 further evaluated 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_FC | p-value | FDR |
|-------------|--------|---------|-----|
| **Up-regulation** | | | |
| HOXC13 | 11.67608 | 1.11×10⁻⁴⁰ | 1.31×10⁻¹⁸ |
| HOXD13 | 11.2923 | 2.95×10⁻²² | 6.08×10⁻¹⁰ |
| KRT31 | 11.18891 | 1.29×10⁻²⁵ | 3.82×10⁻¹⁴ |
| HOXD11 | 11.10495 | 1.02×10⁻³⁴ | 6.57×10⁻²³ |
| ZIC5 | 10.88417 | 5.00×10⁻³¹ | 2.33×10⁻¹⁹ |
| AKR1B15 | 10.8267 | 4.25×10⁻²⁸ | 1.56×10⁻¹⁶ |
| **Down-regulation** | | | |

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| Gene symbol | Log₂ FC | p-value     | FDR          |
|-------------|---------|-------------|--------------|
| RAET1L      | 10.7926 | 7.02×10⁻³³  | 3.89×10⁻³¹   |
| KRTAP4-1    | 10.74082| 4.22×10⁻⁹   | 3.89×10⁻⁸    |
| GNGT1       | 10.7181 | 4.89×10⁻³⁹  | 3.88×10⁻³⁷   |
| DLX6        | 10.55507| 9.98×10⁻³³  | 3.89×10⁻³¹   |
| G12orf5     | 10.50486| 7.72×10⁻⁴⁷  | 1.15×10⁻⁴⁴   |
| SYT14       | 10.42359| 1.39×10⁻²⁸  | 3.89×10⁻²⁶   |
| PITX2       | 10.29313| 7.09×10⁻²⁵  | 1.31×10⁻²³   |
| DSG3        | 10.20777| 5.34×10⁻²³  | 1.75×10⁻²¹   |
| PGLYRP3     | 10.1229 | 1.11×10⁻²³  | 2.67×10⁻²²   |
| TMPRSS11F   | 10.0573 | 1.39×10⁻²³  | 5.98×10⁻²¹   |
| CST4        | 10.00451| 5.48×10⁻³¹  | 1.29×10⁻³⁷   |
| BARX1       | 9.786854| 3.05×10⁻²⁴  | 7.81×10⁻²³   |
| HOXA13      | 9.678895| 4.28×10⁻²⁶  | 1.31×10⁻²⁴   |
| CALM3       | 9.676902| 2.86×10⁻²⁶  | 8.86×10⁻²⁵   |
| DLX6AS      | 9.607182| 8.04×10⁻³⁰  | 3.42×10⁻²⁸   |
| KRT6C       | 9.49044 | 9.95×10⁻³⁸  | 8.11×10⁻³⁶   |
| LUSH1G      | 9.356453| 1.93×10⁻¹⁷  | 1.22×10⁻¹⁶   |
| TERT        | 9.302525| 5.49×10⁻³⁹  | 4.99×10⁻³⁷   |
| C5orf46     | 9.24757 | 3.62×10⁻³³  | 2.08×10⁻³¹   |
| AKR1B10     | 9.050792| 7.46×10⁻²³  | 1.64×10⁻²¹   |
| KRT74       | 9.02461 | 2.30×10⁻²⁶  | 7.16×10⁻²⁵   |
| KRT6B       | 8.990361| 3.06×10⁻³⁵  | 1.28×10⁻³⁴   |
| SPERT       | 8.966005| 1.20×10⁻⁵⁵  | 8.41×10⁻⁴⁸   |
| GABR3       | 8.930636| 3.48×10⁻⁵⁵  | 2.32×10⁻⁴⁸   |
| LOC3339674  | 8.840758| 8.47×10⁻⁴⁸  | 1.31×10⁻⁴⁵   |
| GabRQ       | 8.765859| 9.34×10⁻²³  | 2.03×10⁻²¹   |
| IL1F5       | 8.758799| 1.98×10⁻⁴⁹  | 4.16×10⁻⁴⁷   |
| ZIC2        | 8.684983| 6.98×10⁻⁴⁸  | 3.87×10⁻⁴⁵   |
| PRAME       | 8.613423| 5.36×10⁻²⁴  | 1.35×10⁻²²   |
| SERPINB5    | 8.306376| 2.04×10⁻⁵²  | 4.15×10⁻⁵⁰   |
| GJB6        | 8.340989| 6.15×10⁻²⁷  | 2.05×10⁻²⁵   |
| DDL3        | 8.234224| 2.29×10⁻²⁵  | 6.62×10⁻²⁴   |
| FOXE1       | 8.228799| 4.91×10⁻²⁴  | 1.24×10⁻²²   |
| NRU         | 8.096627| 6.08×10⁻²⁵  | 1.66×10⁻²³   |
| PNCK        | 8.087377| 1.21×10⁻³²  | 5.93×10⁻³⁰   |
| ABCA12      | 7.947086| 1.81×10⁻³⁷  | 1.46×10⁻³⁵   |
| LOC642587   | 7.735536| 1.09×10⁻³⁵  | 7.66×10⁻³³   |
| FAM131C     | 7.695912| 2.95×10⁻³⁵  | 1.98×10⁻³³   |
| FOXD3       | 7.665217| 5.47×10⁻²⁷  | 1.37×10⁻²⁵   |
| DVWA        | 7.626607| 2.90×10⁻³⁰  | 1.28×10⁻₂⁸   |
| DQX1        | 7.587993| 6×10⁻⁴⁶     | 7.37×10⁻⁴²   |
| Gene symbol | Log_{2} FC | p-value          | FDR          |
|-------------|------------|-----------------|--------------|
| KRT5        | 7.513929   | 2.84 \times 10^{-26} | 8.78 \times 10^{-25} |
| TRUS9       | 7.337122   | 2.55 \times 10^{-27} | 3.17 \times 10^{-26} |
| GUC1A       | 7.312747   | 1.47 \times 10^{-27} | 5.14 \times 10^{-26} |
| PITX1       | 7.178973   | 2.40 \times 10^{-51} | 4.65 \times 10^{-49} |
| GUCA1A      | 7.163410   | 5.74 \times 10^{-37} | 5.23 \times 10^{-37} |
| CA9         | 7.14797    | 2.94 \times 10^{-22} | 6.07 \times 10^{-21} |
| COL11A1     | 7.114174   | 5.99 \times 10^{-29} | 2.40 \times 10^{-27} |
| GPR87       | 7.083454   | 3.58 \times 10^{-25} | 1.01 \times 10^{-23} |
| DUSP9       | 7.058347   | 7.88 \times 10^{-40} | 7.53 \times 10^{-38} |
| RAB3B       | 6.992656   | 1.56 \times 10^{-43} | 1.71 \times 10^{-40} |
| GUCA1A      | 6.972018   | 5.07 \times 10^{-39} | 4.63 \times 10^{-37} |
| FAT2        | 6.952899   | 3.61 \times 10^{-27} | 1.24 \times 10^{-25} |
| DUSP9       | 6.932368   | 5.04 \times 10^{-26} | 1.64 \times 10^{-24} |
| GAL         | 6.903164   | 5.41 \times 10^{-26} | 1.64 \times 10^{-24} |
| RIMS2       | 6.899926   | 8.58 \times 10^{-34} | 5.09 \times 10^{-32} |
| MMP12       | 6.886362   | 3.19 \times 10^{-27} | 3.23 \times 10^{-25} |
| DUSP9       | 6.820359   | 1.51 \times 10^{-24} | 3.99 \times 10^{-23} |
| S100A2      | 6.034598   | 9.51 \times 10^{-25} | 2.56 \times 10^{-23} |
| OTX1        | 5.913971   | 1.71 \times 10^{-36} | 1.29 \times 10^{-34} |
| PTHLH       | 5.91066    | 5.97 \times 10^{-24} | 1.49 \times 10^{-22} |
| GJIB        | 5.910017   | 1.73 \times 10^{-28} | 6.39 \times 10^{-26} |
| TAF2A       | 5.898686   | 1.99 \times 10^{-57} | 4.75 \times 10^{-55} |
| ZNF695      | 5.857676   | 3.04 \times 10^{-24} | 7.81 \times 10^{-23} |
| CREM        | 5.84455    | 9.58 \times 10^{-24} | 2.32 \times 10^{-22} |
| KREMEN2     | 5.813638   | 1.98 \times 10^{-21} | 4.62 \times 10^{-22} |
| DLX5        | 5.743708   | 1.04 \times 10^{-31} | 5.16 \times 10^{-30} |
| KRT15       | 5.703738   | 2.04 \times 10^{-21} | 4.27 \times 10^{-20} |
| TMPRSS4     | 5.681538   | 8.78 \times 10^{-31} | 4.03 \times 10^{-29} |
| SLC2A1      | 5.608247   | 1.03 \times 10^{-65} | 3.20 \times 10^{-59} |
| SHOX2       | 5.549365   | 5.29 \times 10^{-25} | 2.28 \times 10^{-23} |
| TNS4        | 5.489393   | 2.16 \times 10^{-28} | 8.16 \times 10^{-27} |
| NAIN1       | 5.44117    | 1.62 \times 10^{-25} | 4.76 \times 10^{-24} |
| CDC45       | 5.396201   | 5.31 \times 10^{-24} | 6.82 \times 10^{-23} |
| CASKIN1     | 5.394552   | 4.73 \times 10^{-23} | 1.06 \times 10^{-21} |
| GJB2        | 5.375627   | 1.68 \times 10^{-25} | 4.94 \times 10^{-24} |
| Gene symbol | Log FC | p-value | FDR  |
|------------|--------|---------|------|
| MMP11      | 5.30769| 5.44×10^-32 | 2.80×10^-30 |
| BIRC5      | 5.262464| 6.28×10^-75 | 1.07×10^-71 |
| RASAL1     | 5.236534| 2.17×10^-34 | 1.36×10^-32 |
| TTK        | 5.181987| 1.19×10^-21 | 8.22×10^-21 |
| HOXA10     | 5.180499| 3.17×10^-28 | 1.18×10^-26 |
| CENPA      | 5.158077| 6.59×10^-24 | 7.96×10^-21 |
| MYBL2      | 5.148039| 1.16×10^-30 | 5.80×10^-27 |
| TROAP      | 5.13211 | 1.71×10^-24 | 2.70×10^-21 |
| WDR72      | 5.108763| 4.78×10^-25 | 1.32×10^-23 |
| UBE2C      | 5.10116 | 1.60×10^-27 | 5.46×10^-24 |
| NEIL3      | 5.08349 | 1.45×10^-46 | 2.09×10^-44 |
| KIF4A      | 5.053856| 7.81×10^-81 | 1.60×10^-76 |
| LRRP3      | 5.046972| 3.12×10^-67 | 1.38×10^-65 |
| POLQ       | 4.995522| 2.51×10^-64 | 9.90×10^-62 |
| TMEM40     | 4.975923| 2.30×10^-26 | 7.16×10^-25 |
| HOX11V     | 4.970191| 8.12×10^-51 | 8.84×10^-48 |
| HIURP      | 4.97107 | 1.74×10^-40 | 1.78×10^-37 |
| DLGAP5     | 4.944602| 1.58×10^-69 | 1.12×10^-66 |
| BUB1B      | 4.937934| 1.27×10^-70 | 2.22×10^-66 |
| NUF2       | 4.928634| 1.70×10^-71 | 1.52×10^-68 |
| TRIM29     | 4.926113| 3.76×10^-25 | 1.05×10^-23 |
| TPRD3      | 4.912277| 6.74×10^-61 | 2.11×10^-58 |
| TPX2       | 4.886094| 3.20×10^-78 | 1.64×10^-74 |
| STRA6      | 4.883579| 2.73×10^-25 | 7.79×10^-24 |
| EX01       | 4.874045| 3.73×10^-90 | 5.10×10^-87 |
| E2F7       | 4.867589| 6.83×10^-39 | 1.78×10^-36 |
| SPC24      | 4.8509  | 1.66×10^-41 | 1.71×10^-39 |
| MELK       | 4.846190| 3.13×10^-66 | 1.49×10^-63 |
| AUERKB     | 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^-61 |
| GJB3       | 4.794771| 1.60×10^-26 | 5.07×10^-23 |
| ALG1L      | 4.783708| 3.24×10^-36 | 2.38×10^-34 |
| FOXM1      | 4.758629| 2.36×10^-44 | 9.71×10^-41 |
| CTS51      | 4.755756| 8.30×10^-44 | 9.85×10^-41 |
| DEPDC1B    | 4.727546| 9.84×10^-65 | 4.21×10^-62 |
| FGF11      | 4.713897| 4.72×10^-81 | 4.71×10^-78 |
| RAD54L     | 4.714778| 1.81×10^-21 | 1.54×10^-18 |
| ARTN       | 4.706166| 1.57×10^-28 | 6.00×10^-25 |
| Gene symbol | Log 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^{-62} | 1.60×10^{-59} |
| EPR1        | 4.615642 | 1.28×10^{-62} | 4.70×10^{-60} |
| ANLN        | 4.59067  | 2.46×10^{-59} | 1.36×10^{-57} |
| KIF2C       | 4.59067  | 1.31×10^{-62} | 2.99×10^{-60} |
| C15orf42    | 4.583778 | 4.02×10^{-56} | 9.07×10^{-54} |
| SLCO4A5     | 4.575648 | 1.71×10^{-62} | 4.36×10^{-60} |
| ASPM        | 4.558095 | 2.41×10^{-62} | 8.49×10^{-60} |
| MCM10       | 4.534639 | 2.73×10^{-66} | 7.38×10^{-64} |
| SKA1        | 4.503986 | 5.42×10^{-62} | 1.79×10^{-60} |
| PKMYT1      | 4.50008  | 3.21×10^{-62} | 9.42×10^{-60} |
| CENPF       | 4.448949 | 2.95×10^{-58} | 7.29×10^{-56} |
| NAP1        | 4.43961  | 7.55×10^{-57} | 1.98×10^{-55} |
| NCAPH       | 4.405723 | 1.02×10^{-67} | 9.52×10^{-65} |
| MND1        | 4.363921 | 1.40×10^{-39} | 3.89×10^{-37} |
| CEP59       | 4.35108  | 3.33×10^{-32} | 9.58×10^{-30} |
| CENPF       | 4.346762 | 5.06×10^{-57} | 1.17×10^{-55} |
| B3GNT4      | 4.327802 | 5.06×10^{-25} | 1.40×10^{-23} |
| TRIP13      | 4.315994 | 2.00×10^{-67} | 4.16×10^{-65} |
| 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 | 1.14×10^{-32} | 3.15×10^{-30} |
| SGOL1       | 4.284447 | 1.14×10^{-32} | 3.15×10^{-30} |
| UHRF1       | 4.282768 | 2.52×10^{-39} | 6.89×10^{-37} |
| SKA3        | 4.277808 | 3.24×10^{-62} | 2.15×10^{-60} |
| NDC80       | 4.26936 | 8.77×10^{-61} | 2.65×10^{-59} |
| PLK1        | 4.263159 | 6.53×10^{-77} | 1.68×10^{-73} |
| CEP59       | 4.259622 | 1.43×10^{-38} | 3.62×10^{-36} |
| C16orf59    | 4.220699 | 7.47×10^{-66} | 2.13×10^{-64} |
| CDC6        | 4.214385 | 1.59×10^{-62} | 5.72×10^{-60} |
| ALDH3B2     | 4.176635 | 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} |
| EPN2        | 4.154454 | 1.28×10^{-54} | 1.04×10^{-52} |
| DSP         | 4.139318 | 2.57×10^{-67} | 3.88×10^{-65} |
| KIF15       | 4.131404 | 2.94×10^{-56} | 6.70×10^{-54} |
| CENPF       | 4.118732 | 1.88×10^{-55} | 4.71×10^{-53} |
| RRM2        | 4.110526 | 3.67×10^{-69} | 9.92×10^{-67} |
| ORC6L       | 4.096011 | 2.35×10^{-66} | 1.17×10^{-64} |
| Gene symbol | Log 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 | 1.39×10^{-75} | 2.60×10^{-72} |
| CDCAS      | 4.067312 | 2.44×10^{-62} | 8.49×10^{-60} |
| SKC25      | 4.017253 | 7.31×10^{-63} | 2.73×10^{-60} |
| KIF20A     | 4.011587 | 3.78×10^{-63} | 1.46×10^{-60} |
| FERMT1     | 3.968932 | 5.24×10^{-63} | 3.14×10^{-59} |
| CCNA2      | 3.960237 | 1.14×10^{-65} | 5.21×10^{-62} |
| KIF4B      | 3.955245 | 7.31×10^{-63} | 2.73×10^{-60} |
| FAM83D     | 3.928708 | 5.44×10^{-63} | 2.07×10^{-60} |
| IQGAP3     | 3.89972  | 1.47×10^{-51} | 3.12×10^{-48} |
| ESCO2      | 3.886113 | 1.15×10^{-54} | 2.52×10^{-51} |
| CDCAS      | 3.872866 | 4.11×10^{-70} | 3.12×10^{-67} |
| C1orf135   | 3.851428 | 1.32×10^{-67} | 7.77×10^{-64} |
| AK3L1      | 3.850189 | 6.67×10^{-64} | 8.73×10^{-61} |
| KIAA0101   | 3.8051   | 1.11×10^{-46} | 1.62×10^{-43} |
| CDK1       | 3.801386 | 4.44×10^{-30} | 6.96×10^{-27} |
| UBE2T      | 3.792088 | 5.39×10^{-62} | 1.79×10^{-59} |
| FBXO43     | 3.78562  | 3.26×10^{-30} | 1.43×10^{-28} |
| CDK3       | 3.771015 | 4.21×10^{-48} | 6.65×10^{-45} |
| HELL5      | 3.744593 | 3.17×10^{-60} | 9.42×10^{-57} |
| CBLC       | 3.729905 | 1.21×10^{-31} | 5.94×10^{-28} |
| KIF11      | 3.703491 | 1.11×10^{-49} | 8.13×10^{-46} |
| XRCC2      | 3.692712 | 1.11×10^{-50} | 2.08×10^{-48} |
| RAD51      | 3.678599 | 3.82×10^{-67} | 2.06×10^{-64} |
| CDCAS      | 3.678311 | 7.55×10^{-48} | 7.41×10^{-45} |
| GINS2      | 3.676896 | 2.62×10^{-53} | 5.44×10^{-50} |
| BRIP1      | 3.664418 | 3.37×10^{-49} | 5.72×10^{-46} |
| BUB1       | 3.652721 | 6.80×10^{-45} | 2.21×10^{-42} |
| PRC1       | 3.633278 | 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 | Log₂FC | p-value | FDR |
|-------------|---------|---------|-----|
| CASC5       | 3.600462| 9.91×10⁻⁵¹ | 1.87×10⁻⁴³ |
| E2F3        | 3.582266| 1.09×10⁻⁴⁶ | 5.61×10⁻⁴⁴ |
| CCNB1       | 3.576527| 2.62×10⁻⁵² | 5.28×10⁻⁵⁰ |
| C17orf53    | 3.567663| 4.19×10⁻⁵⁸ | 8.56×10⁻⁵⁶ |
| MAD2L1      | 3.561721| 1.06×10⁻⁵⁸ | 2.73×10⁻⁵⁶ |
| KIFC1       | 3.553172| 4.27×10⁻⁴⁹ | 1.14×10⁻⁴⁶ |
| EME1        | 3.548072| 9.18×10⁻⁴⁷ | 1.87×10⁻⁴⁴ |
| C17orf53    | 3.546263| 2.62×10⁻⁵² | 5.28×10⁻⁵⁰ |
| ESPN        | 3.540866| 4.19×10⁻⁵⁸ | 8.56×10⁻⁵⁶ |
| MAD2L1      | 3.536894| 1.06×10⁻⁵⁸ | 2.73×10⁻⁵⁶ |
| KIFC1       | 3.530721| 4.27×10⁻⁴⁹ | 1.14×10⁻⁴⁶ |
| EME1        | 3.525623| 9.18×10⁻⁴⁷ | 1.87×10⁻⁴⁴ |
| C17orf53    | 3.523763| 2.62×10⁻⁵² | 5.28×10⁻⁵⁰ |
| MAD2L1      | 3.519894| 1.06×10⁻⁵⁸ | 2.73×10⁻⁵⁶ |
| KIFC1       | 3.513821| 4.27×10⁻⁴⁹ | 1.14×10⁻⁴⁶ |
| EME1        | 3.508723| 9.18×10⁻⁴⁷ | 1.87×10⁻⁴⁴ |
| C17orf53    | 3.506863| 2.62×10⁻⁵² | 5.28×10⁻⁵⁰ |
| MAD2L1      | 3.502994| 1.06×10⁻⁵⁸ | 2.73×10⁻⁵⁶ |
| KIFC1       | 3.496921| 4.27×10⁻⁴⁹ | 1.14×10⁻⁴⁶ |
| EME1        | 3.491823| 9.18×10⁻⁴⁷ | 1.87×10⁻⁴⁴ |
| C17orf53    | 3.488963| 2.62×10⁻⁵² | 5.28×10⁻⁵⁰ |
| MAD2L1      | 3.485194| 1.06×10⁻⁵⁸ | 2.73×10⁻⁵⁶ |
| KIFC1       | 3.480221| 4.27×10⁻⁴⁹ | 1.14×10⁻⁴⁶ |
| EME1        | 3.475123| 9.18×10⁻⁴⁷ | 1.87×10⁻⁴⁴ |
| C17orf53    | 3.472263| 2.62×10⁻⁵² | 5.28×10⁻⁵⁰ |
| MAD2L1      | 3.468494| 1.06×10⁻⁵⁸ | 2.73×10⁻⁵⁶ |
| Gene symbol  | LogFC     | p-value          | FDR            |
|-------------|-----------|------------------|----------------|
| PIF1        | 3.099859  | 3.88×10⁻³³      | 2.21×10⁻⁴⁰    |
| TGFBR2      | 3.076615  | 1.15×10⁻³⁶      | 2.34×10⁻⁴⁰    |
| CARD14      | 3.076131  | 4.59×10⁻²³      | 1.03×10⁻²³    |
| C12orf48    | 3.071974  | 2.60×10⁻⁴²      | 2.80×10⁻⁴⁰    |
| FANCI       | 3.071900  | 1.69×10⁻⁴¹      | 3.72×10⁻⁴³    |
| ARHGAP11A   | 3.057951  | 1.08×10⁻⁴²      | 2.11×10⁻⁴⁹    |
| PTTG1       | 3.056546  | 4.20×10⁻⁵⁷      | 9.80×10⁻⁵⁵    |
| CT2         | 3.037686  | 6.06×10⁻⁴⁴      | 7.36×10⁻⁴²    |
| MLF1IP       | 2.989280  | 5.12×10⁻⁴³      | 5.74×10⁻⁴¹    |
| MCM4         | 2.985368  | 4.08×10⁻⁵⁷      | 9.62×10⁻⁵⁵    |
| PLEKHG6      | 2.976131  | 4.59×10⁻²³      | 1.03×10⁻²³    |
| ARID2        | 2.937900  | 1.95×10⁻⁴³      | 3.88×10⁻⁴³    |
| DNA2         | 2.869444  | 3.03×10⁻⁴³      | 3.43×10⁻⁴³    |
| NFKBIL2      | 2.864318  | 6.18×10⁻³⁵      | 4.06×10⁻³³    |
| C5orf34      | 2.85051   | 1.45×10⁻⁴³      | 1.00×10⁻⁴³    |
| SHCBP1       | 2.85255   | 2.05×10⁻⁴⁵      | 2.75×10⁻⁴³    |
| GYLT1B       | 2.851155  | 1.08×10⁻²²      | 2.33×10⁻²¹    |
| DTL          | 2.840104  | 3.07×10⁻⁴³      | 9.17×10⁻⁴³    |
| RAD54B       | 2.833386  | 8.52×10⁻⁵¹      | 1.62×10⁻⁴⁸    |
| C9orf100     | 2.82468   | 2.62×10⁻³⁵      | 1.76×10⁻³³    |
| LBR          | 2.80509   | 1.09×10⁻²⁵      | 2.36×10⁻²⁶    |
| 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  | 4.15×10⁻⁴⁴      | 9.46×10⁻⁴⁴    |
| CHEK1        | 2.746504  | 2.41×10⁻⁴³      | 5.05×10⁻⁴¹    |
| MARK1        | 2.727147  | 8.69×10⁻²³      | 1.90×10⁻²¹    |
| HMGA1        | 2.726709  | 1.31×10⁻⁴⁶      | 1.91×10⁻⁴⁶    |
| CCNE2        | 2.726381  | 7.49×10⁻³⁴      | 4.47×10⁻³²    |
| GSG2         | 2.724667  | 4.49×10⁻³⁸      | 3.76×10⁻³⁶    |
| PLK4         | 2.703752  | 3.47×10⁻⁵⁰      | 6.20×10⁻⁵⁰    |
| SIX4         | 2.705223  | 8.25×10⁻⁵¹      | 3.81×10⁻⁵⁹    |
| SPTBN2       | 2.698714  | 4.14×10⁻⁴⁶      | 1.27×10⁻⁴⁴    |
| TVM5         | 2.682180  | 2.71×10⁻⁴⁵      | 1.58×10⁻⁴⁵    |
| PPAP2C       | 2.676826  | 2.01×10⁻²⁴      | 5.24×10⁻²³    |
| DSCC1        | 2.6475    | 1.86×10⁻⁴¹      | 1.90×10⁻⁴⁹    |
| ATAD5        | 2.623302  | 4.51×10⁻⁴⁴      | 2.37×10⁻⁴⁴    |
| GPT2         | 2.606793  | 1.43×10⁻²⁸      | 5.48×10⁻²⁷    |
| PYCR1        | 2.597461  | 3.14×10⁻⁴⁵      | 8.87×10⁻⁴⁰    |
| CCNF         | 2.581835  | 2.80×10⁻⁴⁰      | 5.13×10⁻⁴⁰    |
| DDX12        | 2.579215  | 4.42×10⁻²²      | 9.02×10⁻²¹    |
| SLC16A1      | 2.57404   | 3.27×10⁻²⁴      | 8.38×10⁻²³    |

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| Gene symbol | Log_{2} FC | p-value | FDR |
|-------------|------------|---------|-----|
| TRAIP       | 2.572849   | 9.94×10^{-47} | 1.47×10^{-44} |
| NMAP6       | 2.558123   | 4.11×10^{-42} | 3.59×10^{-39} |
| TMEM79      | 2.542757   | 1.20×10^{-23} | 4.86×10^{-21} |
| CCDC34      | 2.528606   | 4.85×10^{-42} | 5.11×10^{-40} |
| TRIM54A     | 2.523846   | 1.42×10^{-24} | 9.86×10^{-22} |
| GRHL1       | 2.518191   | 2.84×10^{-22} | 5.87×10^{-21} |
| CDK5R1      | 2.504349   | 1.88×10^{-25} | 5.48×10^{-24} |
| WDHD1       | 2.497176   | 7.88×10^{-43} | 8.72×10^{-41} |
| CDCA4       | 2.491776   | 8.31×10^{-41} | 8.12×10^{-39} |
| GGH         | 2.469316   | 9.20×10^{-29} | 3.61×10^{-27} |
| CENPH       | 2.466716   | 2.00×10^{-42} | 2.16×10^{-40} |
| KLC1        | 2.458122   | 2.65×10^{-24} | 2.65×10^{-22} |
| KPN5A2      | 2.450852   | 7.10×10^{-48} | 1.0×10^{-45}  |
| SKP2        | 2.429954   | 2.76×10^{-27} | 9.51×10^{-26} |
| KIF18A      | 2.39708    | 1.02×10^{-34} | 6.57×10^{-33} |
| GPRIN1      | 2.37562    | 2.62×10^{-22} | 5.43×10^{-21} |
| MCM8        | 2.358287   | 2.27×10^{-38} | 1.95×10^{-36} |
| BOP1        | 2.356677   | 6.98×10^{-25} | 1.90×10^{-23} |
| SRPS4A1     | 2.355014   | 3.51×10^{-22} | 1.63×10^{-20} |
| CKS1B       | 2.349225   | 1.72×10^{-35} | 1.18×10^{-33} |
| RACGAP1     | 2.345876   | 2.26×10^{-48} | 3.60×10^{-46} |
| MCM6        | 2.340356   | 1.23×10^{-26} | 4.24×10^{-24} |
| HMGBO3      | 2.328465   | 3.03×10^{-24} | 7.80×10^{-22} |
| MFS2B       | 2.318549   | 9.42×10^{-24} | 2.29×10^{-22} |
| ATAD2       | 2.317108   | 4.12×10^{-48} | 4.09×10^{-46} |
| LOC100125556| 2.313755   | 6.12×10^{-31} | 3.42×10^{-30} |
| C1orf74     | 2.286936   | 4.67×10^{-30} | 2.02×10^{-28} |
| TIMELESS    | 2.264996   | 1.13×10^{-31} | 1.31×10^{-29} |
| RCC1        | 2.259865   | 2.44×10^{-39} | 2.28×10^{-37} |
| C1orf112    | 2.259727   | 6.31×10^{-38} | 5.16×10^{-36} |
| PKD2        | 2.249799   | 7.20×10^{-32} | 2.37×10^{-30} |
| AURKAP51    | 2.223938   | 5.47×10^{-25} | 1.50×10^{-23} |
| NCAPG2      | 2.220921   | 1.22×10^{-36} | 9.40×10^{-35} |
| ACTL6A      | 2.184197   | 1.44×10^{-20} | 5.99×10^{-19} |
| FANCA       | 2.16958    | 7.75×10^{-28} | 2.77×10^{-26} |
| CHEK2       | 2.164867   | 4.11×10^{-31} | 1.93×10^{-29} |
| TP53        | 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} |

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| Gene symbol   | Log_{2} FC | p-value    | FDR       |
|--------------|------------|------------|-----------|
| C11orf82     | 2.125601   | 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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 × 36 |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| LOC100128191 | 2.096295   | 1.89 × 10^{-28} | 7.19 × 10^{-27} |
| 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} |
| GMP1       | 1.85722    | 3.85×10^{-32}  | 1.81×10^{-30} |
| CENPN      | 1.849211   | 1.29×10^{-24}  | 3.44×10^{-23} |
| E2F1       | 1.840214   | 5.32×10^{-25}  | 1.49×10^{-23} |
| TFAP4      | 1.839016   | 1.07×10^{-26}  | 3.44×10^{-25} |
| ALG3       | 1.838391   | 1.29×10^{-24}  | 3.44×10^{-23} |
| GMP1       | 1.837272   | 1.07×10^{-26}  | 3.44×10^{-25} |
| CENPN      | 1.839211   | 1.29×10^{-24}  | 3.44×10^{-23} |
| E2F1       | 1.838016   | 5.32×10^{-25}  | 1.49×10^{-23} |
| TFAP4      | 1.839016   | 1.07×10^{-26}  | 3.44×10^{-25} |
| ALG3       | 1.838391   | 1.29×10^{-24}  | 3.44×10^{-23} |
| GMP1       | 1.837272   | 1.07×10^{-26}  | 3.44×10^{-25} |

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| Gene symbol | Log_FC | p-value | FDR   |
|-------------|--------|---------|-------|
| CCT5        | 1.655027 | 1.25x10^-29 | 5.23x10^-28 |
| RANBP1      | 1.654887 | 6.50x10^-10 | 1.14x10^-26 |
| DKC1        | 1.633363 | 6.84x10^-32 | 3.47x10^-30 |
| SUV39H2     | 1.628626 | 5.34x10^-27 | 1.79x10^-25 |
| XPOT        | 1.623617 | 2.56x10^-28 | 7.94x10^-25 |
| C3orf26     | 1.612231 | 6.70x10^-24 | 1.67x10^-22 |
| COQ3        | 1.602896 | 1.08x10^-23 | 3.21x10^-22 |
| UNG         | 1.596097 | 2.84x10^-24 | 1.49x10^-29 |
| TPI1        | 1.578752 | 4.03x10^-28 | 1.24x10^-24 |
| C12orf11    | 1.569481 | 7.47x10^-32 | 3.76x10^-30 |
| MRPL47      | 1.552328 | 2.12x10^-22 | 4.44x10^-21 |
| ZFP64       | 1.559335 | 4.91x10^-32 | 2.54x10^-30 |
| MTHR1       | 1.533402 | 8.39x10^-33 | 4.65x10^-31 |
| DDX39       | 1.51532  | 4.41x10^-22 | 8.99x10^-21 |
| C2orf20     | 1.549278 | 4.98x10^-34 | 3.00x10^-32 |
| TOPBP1      | 1.54732  | 5.83x10^-24 | 2.73x10^-33 |
| RUVBL1      | 1.538438 | 4.95x10^-29 | 1.99x10^-27 |
| HPRT1       | 1.535165 | 9.56x10^-25 | 3.21x10^-24 |
| MC35        | 1.523754 | 4.06x10^-21 | 9.17x10^-22 |
| DTYMK       | 1.518073 | 4.07x10^-23 | 9.19x10^-22 |
| NIPSNAP1    | 1.503167 | 8.94x10^-24 | 2.18x10^-22 |
| CCDC99      | 1.500315 | 5.71x10^-28 | 2.07x10^-26 |
| PSMG3       | 1.500262 | 4.33x10^-24 | 1.09x10^-26 |
| RRM1        | 1.498123 | 2.26x10^-22 | 4.72x10^-21 |
| PRM2        | 1.497858 | 1.66x10^-24 | 4.36x10^-23 |
| DPR1        | 1.493721 | 8.45x10^-21 | 1.85x10^-20 |
| SSX2IP      | 1.478768 | 1.76x10^-22 | 3.71x10^-21 |
| WDR53       | 1.475187 | 4.87x10^-23 | 3.71x10^-21 |
| CCDC21      | 1.472299 | 2.22x10^-22 | 4.64x10^-21 |
| SNRP4       | 1.469144 | 1.61x10^-32 | 8.62x10^-31 |
| CSE1L       | 1.461911 | 4.29x10^-37 | 3.34x10^-35 |
| JAK2        | 1.459939 | 2.12x10^-41 | 6.13x10^-38 |
| WDR67       | 1.45802  | 3.74x10^-25 | 1.05x10^-23 |
| TIMM8A      | 1.457409 | 1.87x10^-22 | 3.94x10^-21 |
| RAE1        | 1.457254 | 6.13x10^-23 | 4.43x10^-21 |
| KIF22       | 1.450715 | 1.56x10^-24 | 4.13x10^-23 |
| C10orf2     | 1.438043 | 9.56x10^-24 | 2.32x10^-22 |
| Gene symbol | Log_{2} FC | p-value | FDR       |
|-------------|------------|---------|-----------|
| RFWD3       | 1.43459    | 2.11×10^{-28} | 8.00×10^{-27} |
| CPOX        | 1.424399   | 2.66×10^{-24} | 6.87×10^{-23} |
| SRPK1       | 1.420745   | 5.62×10^{-31} | 2.61×10^{-29} |
| TMEM68      | 1.420100   | 5.64×10^{-31} | 2.61×10^{-29} |
| DCAF13      | 1.418586   | 3.15×10^{-32} | 1.50×10^{-29} |
| HSPD1       | 1.416285   | 1.47×10^{-24} | 3.90×10^{-23} |
| 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} |
| TMEM68      | 1.420100   | 5.64×10^{-31} | 2.61×10^{-29} |
| DCAF13      | 1.418586   | 3.15×10^{-32} | 1.50×10^{-29} |
| HSPD1       | 1.416285   | 1.47×10^{-24} | 3.90×10^{-23} |
| C1orf32     | 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   | 3.89×10^{-27} | 1.32×10^{-25} |
| 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} | 1.50×10^{-22} |
| CCDC86      | 1.348674   | 2.35×10^{-24} | 6.77×10^{-23} |
| DNAJC9      | 1.340408   | 8.53×10^{-23} | 3.31×10^{-22} |
| NUP37       | 1.335745   | 3.94×10^{-30} | 1.72×10^{-28} |
| PRMT3       | 1.332288   | 9.79×10^{-23} | 2.13×10^{-21} |
| C1orf131    | 1.330127   | 1.36×10^{-24} | 3.61×10^{-23} |
| DUS4L       | 1.329328   | 4.50×10^{-24} | 1.86×10^{-22} |
| B4GALT2     | 1.322937   | 9.35×10^{-25} | 4.25×10^{-23} |
| NAA50       | 1.310484   | 4.29×10^{-25} | 2.09×10^{-23} |
| 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^{-24} | 1.38×10^{-23} |
| NOP56       | 1.283091   | 1.02×10^{-21} | 2.47×10^{-22} |
| METAP1      | 1.272501   | 1.05×10^{-22} | 2.28×10^{-21} |
| YWHAZ       | 1.271744   | 1.27×10^{-22} | 2.72×10^{-21} |
| WDR75       | 1.253088   | 2.60×10^{-25} | 7.46×10^{-24} |
| OLA1        | 1.247661   | 1.13×10^{-20} | 2.44×10^{-20} |
| 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^{-23} | 4.71×10^{-22} |
| TH1L        | 1.228534   | 4.96×10^{-24} | 1.25×10^{-22} |
| ALDH18A1    | 1.227343   | 4.89×10^{-31} | 2.29×10^{-29} |
| FAM136A     | 1.223441   | 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} |

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[ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]
| Gene symbol | Log_{2} FC | p-value   | FDR        |
|-------------|------------|-----------|------------|
| MTIF2       | 1.213798   | 1.33 \times 10^{-26} | 4.27 \times 10^{-25} |
| TUBB        | 1.203656   | 2.31 \times 10^{-23} | 5.54 \times 10^{-22} |
| FAM189B     | 1.197619   | 5.38 \times 10^{-23} | 1.20 \times 10^{-21} |
| HN1L        | 1.193616   | 4.83 \times 10^{-24} | 1.22 \times 10^{-22} |
| TRAP1       | 1.190945   | 3.01 \times 10^{-21} | 6.18 \times 10^{-20} |
| HDGF        | 1.188787   | 2.04 \times 10^{-27} | 7.09 \times 10^{-26} |
| R3HDM1      | 1.17991    | 6.86 \times 10^{-24} | 1.70 \times 10^{-22} |
| XPO1        | 1.161185   | 2.32 \times 10^{-23} | 5.35 \times 10^{-22} |
| SLC25A39    | 1.140258   | 2.78 \times 10^{-22} | 5.75 \times 10^{-21} |
| HDAC1       | 1.129796   | 6.97 \times 10^{-24} | 1.72 \times 10^{-22} |
| INTS8       | 1.129134   | 7 \times 10^{-24}    | 1.75 \times 10^{-22} |
| TMEM69      | 1.115962   | 3.67 \times 10^{-26} | 1.13 \times 10^{-24} |
| TRAF7       | 1.10877    | 7.67 \times 10^{-23} | 1.69 \times 10^{-21} |
| NQO1        | 1.077903   | 8.73 \times 10^{-26} | 2.68 \times 10^{-24} |
| PALB2       | 1.061808   | 1.82 \times 10^{-21} | 4.27 \times 10^{-22} |
| CPSF3       | 1.05951    | 5.15 \times 10^{-23} | 1.15 \times 10^{-21} |
| HN1L        | 1.05742    | 1.01 \times 10^{-22} | 2.54 \times 10^{-21} |
| PRPF19      | 1.045652   | 3.00 \times 10^{-29} | 1.23 \times 10^{-27} |
| PSMID12     | 1.035337   | 4.44 \times 10^{-22} | 9.04 \times 10^{-21} |
| PPM1G       | 0.98628    | 1.01 \times 10^{-21} | 2.58 \times 10^{-21} |
| TAF2        | 0.986898   | 1.37 \times 10^{-21} | 3.26 \times 10^{-22} |
| CCT7        | 0.976101   | 1.48 \times 10^{-22} | 3.15 \times 10^{-21} |
| KCMF1       | 0.937533   | 2.22 \times 10^{-24} | 5.76 \times 10^{-23} |

**Down-regulation**

| Gene symbol | Log_{2} FC | p-value    | FDR        |
|-------------|------------|------------|------------|
| LOC149620   | -12.1594   | 2.40 \times 10^{-27} | 8.31 \times 10^{-26} |
| CYP2A2      | -9.76271   | 1.98 \times 10^{-28} | 4.63 \times 10^{-28} |
| CAV3        | -9.34724   | 3.51 \times 10^{-28} | 1.08 \times 10^{-27} |
| OTC         | -9.08217   | 1.61 \times 10^{-22} | 3.42 \times 10^{-21} |
| CLDN18      | -8.69473   | 5.95 \times 10^{-28} | 2.15 \times 10^{-27} |
| LOC572558   | -8.66928   | 1.46 \times 10^{-26} | 4.65 \times 10^{-25} |
| LCN6        | -8.61148   | 8.39 \times 10^{-23} | 1.84 \times 10^{-21} |
| GUC2A       | -8.36433   | 4.32 \times 10^{-21} | 9.27 \times 10^{-21} |
| GP9         | -8.36052   | 4.11 \times 10^{-22} | 8.40 \times 10^{-21} |
| OR6K3       | -8.17655   | 2.75 \times 10^{-29} | 1.13 \times 10^{-27} |
| CELA2B      | -7.98306   | 7.15 \times 10^{-30} | 2.36 \times 10^{-28} |
| HBM         | -7.84657   | 1.22 \times 10^{-31} | 5.96 \times 10^{-30} |
| AGER        | -7.5324    | 3.96 \times 10^{-46} | 5.57 \times 10^{-44} |
| RXF2        | -7.28848   | 4.61 \times 10^{-38} | 3.85 \times 10^{-37} |
| ACSM2A      | -7.19524   | 1.04 \times 10^{-24} | 2.78 \times 10^{-23} |
| GGTL1       | -7.10107   | 4.79 \times 10^{-27} | 1.62 \times 10^{-25} |
| Gene symbol | Log, FC | p-value       | FDR       |
|-------------|---------|---------------|-----------|
| CLEC1B      | -6.89042| 1.58×10^-26   | 5.01×10^-25|
| CLEC3B      | -6.85336| 1.2×10^-24    | 3.12×10^-23|
| MS4A15      | -6.81763| 2.34×10^-22   | 4.87×10^-21|
| CELA2A      | -6.6855  | 1.73×10^-25   | 5.07×10^-24|
| C1orf69     | -6.14884| 1.48×10^-19   | 1.8×10^-18 |
| GP1BP1      | -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^-30      | 1×10^-26  |
| CLIC5       | -6.11393| 1.90×10^-42   | 1.92×10^-39|
| FIGF        | -6.07733| 2.45×10^-28   | 9.23×10^-27|
| FAM107A     | -6.03707| 4.42×10^-41   | 4.70×10^-38|
| HBB         | -5.97249| 1.31×10^-25   | 3.89×10^-24|
| SCUBE1      | -5.93284| 1.11×10^-22   | 2.39×10^-21|
| TMD100      | -5.9153  | 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|
| VEPH1       | -5.64109| 1.67×10^-27   | 5.82×10^-26|
| INMT        | -5.63399| 1.16×10^-43   | 1.34×10^-41|
| MARCO       | -5.5977  | 1.72×10^-55   | 1.53×10^-53|
| HBA2        | -5.47844| 6.69×10^-33   | 3.72×10^-31|
| DES         | -5.46299| 1.94×10^-24   | 5.06×10^-23|
| SUSD2       | -5.45303| 2.0×10^-24    | 1.60×10^-23|
| TNXB        | -5.41186| 2.72×10^-37   | 2.14×10^-35|
| C4orf31     | -5.3604  | 1.31×10^-26   | 4.21×10^-25|
| CELA4       | -5.2613  | 1.67×10^-35   | 2.85×10^-32|
| 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^-17   | 8.10×10^-16|
| 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^-31   | 4.05×10^-29|
| COL4A3      | -4.97118| 1.35×10^-21   | 3.23×10^-22|
| FH15        | -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^-21   | 3.35×10^-22|
| ABCA3       | -4.8312 | 2.03×10^-23   | 4.73×10^-22|
| GVFB        | -4.80865| 1.45×10^-31   | 7.90×10^-30|
| ATOH8       | -4.77835| 3.88×10^-30   | 1.69×10^-28|
| LRRK2       | -4.72852| 1.71×10^-26   | 5.40×10^-25|
| GCOM1       | -4.72599| 2.22×10^-31   | 1.30×10^-29|
| LPL          | -4.6552 | 1.04×10^-31   | 5.14×10^-30|
| PREX2       | -4.59971| 2.77×10^-22   | 5.72×10^-21|
| Gene symbol | Log₂FC | p-value     | FDR          |
|-------------|--------|-------------|--------------|
| MRC1        | -4.59473 | 1.05×10⁻²⁹  | 4.43×10⁻²⁸   |
| C1QTNF7     | -4.57173 | 2.80×10⁻²³  | 6.40×10⁻²²   |
| PDK4        | -4.51265 | 1.00×10⁻²⁶  | 3.25×10⁻²⁵   |
| LVE1        | -4.49974 | 2.27×10⁻²ⁱ  | 1.69×10⁻²⁰   |
| EDNRB       | -4.48935 | 2.39×10⁻²⁸  | 2.04×10⁻²⁷   |
| NPR1        | -4.4785  | 1.11×10⁻²⁸  | 9.80×10⁻²⁷   |
| HSD17B6     | -4.46056 | 9.00×10⁻⁴⁰  | 1.45×10⁻³⁶   |
| CCDC48      | -4.42839 | 2.32×10⁻³⁹  | 2.19×10⁻³⁷   |
| LRRN3       | -4.4158  | 9.76×10⁻²⁴  | 2.36×10⁻²²   |
| AFF3        | -4.39441 | 2.44×10⁻²⁷  | 8.42×10⁻²⁶   |
| HLX         | -4.37102 | 1.40×10⁻³⁵  | 1.21×10⁻³⁴   |
| HIGD1B      | -4.38676 | 1.48×10⁻³²  | 8.01×10⁻³¹   |
| NOSTRIN     | -4.36725 | 4.05×10⁻⁴⁴  | 5.04×10⁻⁴²   |
| FHL1        | -4.33998 | 2.35×10⁻³⁷  | 2.21×10⁻³⁵   |
| STEAP4      | -4.33369 | 1.27×10⁻²²  | 2.72×10⁻²¹   |
| GPR116      | -4.30121 | 1.71×10⁻⁴⁵  | 2.31×10⁻⁴³   |
| SELNBP1     | -4.28341 | 5.03×10⁻³³  | 2.85×10⁻³¹   |
| SYT15       | -4.26624 | 1.13×10⁻²³  | 2.72×10⁻²²   |
| SLC19A3     | -4.23925 | 6.95×10⁻⁴⁷  | 2.29×10⁻³⁶   |
| SDPR        | -4.22143 | 1.08×10⁻⁴⁴  | 1.27×10⁻⁴¹   |
| DLC1        | -4.20133 | 5.11×10⁻⁳³  | 2.89×10⁻³¹   |
| HSPB6       | -4.19155 | 8.63×10⁻⁴⁴  | 5.93×10⁻⁴²   |
| SLC39A8     | -4.19155 | 5.97×10⁻⁴⁴  | 7.29×10⁻⁴²   |
| MFAF4       | -4.17775 | 2.56×10⁻²⁵  | 7.39×10⁻²⁴   |
| AB3B        | -4.14267 | 9.53×10⁻⁴⁵  | 2.56×10⁻⁴³   |
| OLR1        | -4.14203 | 3.94×10⁻²⁵  | 1×10⁻²³      |
| KL          | -4.12562 | 6.31×10⁻²⁵  | 1.73×10⁻²³   |
| EMCN        | -4.10201 | 1.45×10⁻²⁵  | 1.00×10⁻²³   |
| CPAMD8      | -4.06285 | 4.48×10⁻⁰⁵  | 1.25×10⁻³⁵   |
| MMRN1       | -4.05246 | 8.48×10⁻⁰³  | 1.86×10⁻²¹   |
| RTKN2       | -4.04400 | 5.50×10⁻⁰⁶  | 7.68×10⁻⁴⁶   |
| FMO2        | -4.02069 | 8.74×10⁻⁰⁵  | 2.36×10⁻²³   |
| AOC3        | -4.01357 | 1.26×10⁻³⁰  | 7.48×10⁻⁴²   |
| SHE         | -4.00092 | 1.66×10⁻⁰⁵  | 1.25×10⁻²¹   |
| C11orf9     | -4.00034 | 2.69×10⁻²¹  | 6.17×10⁻²²   |
| FBP1        | -3.99803 | 3.06×10⁻²⁹  | 1.25×10⁻²⁷   |
| AKC         | -3.99551 | 5.07×10⁻⁰⁷  | 1.40×10⁻¹⁰   |
| WISP2       | -3.98576 | 7.95×10⁻¹³  | 1.75×10⁻²¹   |
| ABCC6       | -3.94026 | 1.17×10⁻²⁰  | 5.33×10⁻²⁹   |
| Gene symbol | Log₂FC | p-value   | FDR       |
|-------------|--------|-----------|-----------|
| C6orf174    | -3.88844 | 5.79×10⁻²⁶ | 1.76×10⁻²⁴ |
| C5orf57     | -3.83827 | 6.42×10⁻²³ | 1.43×10⁻²⁰ |
| FMOS        | -3.8698 | 2.25×10⁻²⁶ | 7.02×10⁻²³ |
| VSIG4       | -3.86189 | 6.51×10⁻²⁵ | 1.77×10⁻²² |
| ALM1        | -3.87007 | 4.70×10⁻²³ | 3.43×10⁻²⁰ |
| SPOCK2      | -3.84696 | 5.18×10⁻²⁹ | 2.08×10⁻²⁶ |
| CCDC85A     | -3.84811 | 3.00×10⁻²⁸ | 1.12×10⁻²⁵ |
| ARHGAP6     | -3.7906 | 3.67×10⁻³¹ | 1.73×10⁻²⁸ |
| PRX         | -3.79235 | 4.63×10⁻³⁹ | 4.24×10⁻³⁶ |
| SLC1A1      | -3.77875 | 1.58×10⁻³² | 8.50×10⁻²⁹ |
| CD36        | -3.76877 | 8.32×10⁻²³ | 1.83×10⁻²⁰ |
| IFITM5      | -3.7797 | 4.22×10⁻²⁹ | 5.8×10⁻²⁶ |
| S1PR1       | -3.74494 | 3.83×10⁻⁴⁰ | 3.71×10⁻³⁷ |
| SPN         | -3.73016 | 2.72×10⁻²⁹ | 1.12×10⁻²⁶ |
| LUMCH1      | -3.72864 | 4.65×10⁻⁴⁰ | 1.70×10⁻³⁷ |
| AKAP2       | -3.71963 | 1.75×10⁻³⁰ | 7.87×10⁻²⁷ |
| FGFR4       | -3.71134 | 1.39×10⁻²⁶ | 4.44×10⁻²³ |
| TAL1        | -3.70846 | 2.97×10⁻³⁰ | 1.14×10⁻²⁶ |
| ALDH3B1     | -3.69884 | 5.40×10⁻³² | 2.79×10⁻²⁹ |
| KANK3       | -3.69294 | 4.49×10⁻⁴⁹ | 7.43×10⁻⁴⁶ |
| COX4I2      | -3.67548 | 6.09×10⁻⁵⁰ | 2.38×10⁻⁴⁷ |
| CDH5        | -3.67113 | 1.26×10⁻⁴⁴ | 1.61×10⁻⁴¹ |
| CLDN5       | -3.66702 | 1.01×10⁻³⁰ | 4.65×10⁻²⁷ |
| NRGN        | -3.66589 | 2.83×10⁻³⁵ | 8.05×10⁻³² |
| MSR1        | -3.6607 | 8.39×10⁻²⁴ | 2.05×10⁻²¹ |
| DPEP2       | -3.64229 | 4.71×10⁻³⁰ | 2.04×10⁻²⁷ |
| CCK3R1      | -3.62554 | 1.22×10⁻⁴⁰ | 2.92×10⁻³⁷ |
| LOC158376   | -3.62252 | 3.99×10⁻³¹ | 8.05×10⁻²⁸ |
| ARHGGEF15   | -3.61949 | 3.07×10⁻⁴⁴ | 3.89×10⁻⁴¹ |
| SOX17       | -3.61647 | 3.27×10⁻⁴⁷ | 2.56×10⁻⁴⁴ |
| ECSCR       | -3.60883 | 2.05×10⁻³⁷ | 1.63×10⁻³⁴ |
| RICH2       | -3.58888 | 3.16×10⁻³⁰ | 5.26×10⁻²⁷ |
| PRAM1       | -3.58695 | 3.58×10⁻⁴⁰ | 1.33×10⁻³⁷ |
| PTH1R       | -3.58311 | 3.39×10⁻²⁵ | 9.57×10⁻²² |
| CDS2        | -3.58154 | 1.59×10⁻²⁷ | 5.55×10⁻²⁴ |
| C13orf15    | -3.56071 | 1.53×10⁻²⁹ | 2.64×10⁻²⁶ |
| HYAL1       | -3.55975 | 2.04×10⁻⁹⁰ | 9.10×10⁻⁶⁹ |
| VIPR1       | -3.54455 | 3.84×10⁻²⁷ | 1.31×10⁻²⁴ |
| PKN0X2      | -3.54266 | 7.29×10⁻⁷⁰ | 1.79×10⁻⁵⁷ |
| LDB2        | -3.52548 | 5.25×10⁻⁴⁵ | 6.91×10⁻⁴² |
| GLDN        | -3.52371 | 5.12×10⁻²⁹ | 2.06×10⁻²⁶ |
| Gene symbol | Log2 FC | p-value | FDR |
|-------------|---------|---------|-----|
| CGNL1       | -3.52076| 1.23×10^-27 | 4.35×10^-26 |
| F10         | -3.50755| 1.67×10^-22  | 3.53×10^-21 |
| JPH4        | -3.50154| 4.63×10^-22  | 9.40×10^-21 |
| CAV1        | -3.48723| 6×10^-10^-32 | 2.82×10^-29 |
| HOPX        | -3.48553| 5.64×10^-23  | 1.25×10^-21 |
| SEMA3B      | -3.47522| 4.80×10^-30  | 1.24×10^-28 |
| CFP         | -3.46713| 1.13×10^-29  | 4.75×10^-28 |
| PHACTR1     | -3.46399| 2.75×10^-34  | 1.72×10^-32 |
| CDF         | -3.43599| 5.06×10^-30  | 2.18×10^-28 |
| GRPRP1      | -3.42639| 8.46×10^-39  | 7.55×10^-37 |
| C5orf4      | -3.41819| 4.63×10^-32  | 2.40×10^-30 |
| SYNE1       | -3.41118| 1.77×10^-36  | 9.57×10^-34 |
| LAMP3       | -3.40731| 3.70×10^-25  | 1.04×10^-23 |
| KLF2        | -3.40531| 1.46×10^-18  | 1.28×10^-16 |
| ALOX5AP     | -3.40055| 1.40×10^-16  | 1.44×10^-15 |
| VWF         | -3.39482| 3.82×10^-33  | 2.18×10^-31 |
| OSCAR       | -3.39291| 1.17×10^-30  | 5.32×10^-29 |
| GSTM5       | -3.38919| 1.05×10^-28  | 2.30×10^-26 |
| ACVR1L1     | -3.37762| 1.21×10^-45  | 1.66×10^-43 |
| C1orf116    | -3.36689| 4.27×10^-26  | 1.31×10^-24 |
| MUC1        | -3.36508| 2.63×10^-30  | 9.87×10^-28 |
| MS4A7       | -3.36205| 2.55×10^-28  | 7.92×10^-26 |
| ALOX5       | -3.35924| 2.65×10^-15  | 7.58×10^-14 |
| ARRB1       | -3.35891| 3.42×10^-37  | 1.97×10^-35 |
| ESAM        | -3.35409| 2.52×10^-47  | 3.83×10^-45 |
| NLRC4       | -3.35065| 5.43×10^-38  | 4.46×10^-36 |
| GNG11       | -3.35332| 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^-24  | 3.95×10^-22 |
| CD93        | -3.29485| 8.24×10^-15  | 5.35×10^-13 |
| TPPP3       | -3.27648| 2.40×10^-22  | 4.99×10^-21 |
| PDE2A       | -3.27601| 2.88×10^-19  | 8.89×10^-18 |
| CLEC14A     | -3.27085| 7.32×10^-43  | 8.16×10^-41 |
| RAMP2       | -3.25241| 3.56×10^-47  | 5.33×10^-45 |
| AATK        | -3.25144| 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     | -3.22511  | 1.32×10^{-32} | 1.19×10^{-30} |
| RNASE1     | -3.23871  | 6.24×10^{-26} | 4.93×10^{-24} |
| C2orf160   | -3.2263   | 1.34×10^{-35} | 9.35×10^{-34} |
| FUS1P1     | -3.22751  | 1.47×10^{-29} | 1.12×10^{-27} |
| CD300F     | -3.22751  | 1.08×10^{-22} | 2.98×10^{-21} |
| LIMS2      | -3.22121  | 8.40×10^{-33} | 2.33×10^{-32} |
| STARD8     | -3.23871  | 6.24×10^{-26} | 4.93×10^{-24} |
| RNASE1     | -3.2263   | 1.34×10^{-35} | 9.35×10^{-34} |
| C2orf160   | -3.22751  | 1.47×10^{-29} | 1.12×10^{-27} |
| FUS1P1     | -3.22751  | 1.08×10^{-22} | 2.98×10^{-21} |
| LIMS2      | -3.22121  | 8.40×10^{-33} | 2.33×10^{-32} |
| STARD8     | -3.23871  | 6.24×10^{-26} | 4.93×10^{-24} |
| RNASE1     | -3.2263   | 1.34×10^{-35} | 9.35×10^{-34} |
| C2orf160   | -3.22751  | 1.47×10^{-29} | 1.12×10^{-27} |
| FUS1P1     | -3.22751  | 1.08×10^{-22} | 2.98×10^{-21} |
| LIMS2      | -3.22121  | 8.40×10^{-33} | 2.33×10^{-32} |

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| Gene symbol | Log FC | p-value  | FDR    |
|------------|--------|----------|--------|
| GIMAP6     | -2.99933 | 4.50×10^{-26} | 1.37×10^{-24} |
| DUSP2     | -2.98346 | 1.22×10^{-29} | 1.66×10^{-27} |
| DENND2A    | -2.98587 | 1.33×10^{-25} | 3.95×10^{-24} |
| TUBB1      | -2.98462 | 6.32×10^{-35} | 4.13×10^{-33} |
| FAM13C     | -2.98426 | 6.72×10^{-26} | 1.49×10^{-24} |
| C20orf202  | -2.97064 | 1.57×10^{-23} | 3.71×10^{-22} |
| SLC11A1    | -2.96521 | 4.93×10^{-27} | 1.66×10^{-25} |
| PCDH12     | -2.96104 | 1.33×10^{-25} | 3.95×10^{-24} |
| TUBB1      | -2.95853 | 6.41×10^{-25} | 1.75×10^{-23} |
| FAM13C     | -2.94297 | 1.91×10^{-22} | 4.02×10^{-21} |
| SORBS1     | -2.93756 | 1.00×10^{-24} | 2.69×10^{-23} |
| LMO7       | -2.89541 | 7.26×10^{-41} | 1.89×10^{-39} |
| CELF2      | -2.89857 | 4.30×10^{-38} | 3.62×10^{-36} |
| BCL6B      | -2.86159 | 5.21×10^{-28} | 1.71×10^{-26} |
| GRASP      | -2.85483 | 1.69×10^{-24} | 1.44×10^{-23} |
| RPS6KA2     | -2.85267 | 1.53×10^{-28} | 6.34×10^{-26} |
| LOC100302650 | -2.84493 | 7.06×10^{-24} | 1.74×10^{-22} |
| MMRN2 | -2.84444 | 7.13×10^{-33} | 3.06×10^{-31} |
| LEPOR      | -2.86025 | 4.70×10^{-28} | 1.71×10^{-26} |
| MGLL       | -2.79541 | 1.06×10^{-22} | 2.30×10^{-21} |
| GLIPR2     | -2.79478 | 5.14×10^{-28} | 2.90×10^{-26} |
| SGMS2      | -2.78896 | 6.74×10^{-27} | 2.23×10^{-25} |
| IL3RA      | -2.78779 | 2.77×10^{-28} | 1.23×10^{-28} |

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| Gene symbol | Log_FC | p-value | FDR    |
|------------|--------|---------|--------|
| TRPV2      | −2.78591| 2.16×10^−28 | 8.16×10^−27 |
| CD34       | −1.34  | 1.13×10^−10 | 7.21×10^−11 |
| ARHGAP29   | −2.77841| 4.50×10^−22 | 9.16×10^−21 |
| F8         | −2.77365| 8.66×10^−39 | 7.70×10^−37 |
| CVRY1      | −2.76004| 1.26×10^−28 | 8.49×10^−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^−29 | 8.51×10^−28 |
| ACE        | −2.75464| 4.75×10^−29 | 1.92×10^−27 |
| EMP2       | −2.75105| 8.21×10^−35 | 5.35×10^−33 |
| KDR        | −2.73606| 1.11×10^−26 | 3.57×10^−25 |
| CCDC69     | −2.73141| 7.48×10^−25 | 2.03×10^−23 |
| ENG        | −2.7745 | 1.46×10^−28 | 7.21×10^−27 |
| SPNS2      | −2.70412| 4.34×10^−24 | 1.0×10^−22 |
| FLVCR2     | −2.70055| 8.12×10^−24 | 1.99×10^−22 |
| P2RY14     | −2.6932 | 6.86×10^−24 | 1.51×10^−23 |
| AHCYL2     | −2.69886| 1.81×10^−38 | 1.57×10^−36 |
| MFG4       | −2.68354| 9.22×10^−27 | 3.00×10^−25 |
| GRK5       | −2.68108| 1.62×10^−30 | 1.23×10^−28 |
| NRS5A2     | −2.66246| 7.92×10^−27 | 2.60×10^−25 |
| STARD13    | −2.66146| 2.58×10^−27 | 7.41×10^−26 |
| S100A4     | −2.66043| 4.73×10^−27 | 1.60×10^−25 |
| GADD45B    | −2.6507 | 6.50×10^−29 | 2.59×10^−27 |
| CD97       | −2.64755| 9.65×10^−30 | 4.08×10^−28 |
| TEC1       | −2.64161| 2.57×10^−37 | 2.04×10^−35 |
| FLT4       | −2.6282 | 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 |
| CDH3       | −2.61125| 1.82×10^−30 | 5.72×10^−28 |
| FZD4       | −2.61125| 7.71×10^−34 | 4.59×10^−32 |
| SPI1       | −2.61005| 3.72×10^−22 | 7.63×10^−21 |
| CDS5       | −2.59833| 7.24×10^−29 | 3.08×10^−27 |
| ZFP36      | −2.59747| 1.90×10^−21 | 4.45×10^−22 |
| DENND3     | −2.58669| 2.34×10^−27 | 8.09×10^−26 |
| KANK2      | −2.58518| 5.25×10^−21 | 4.33×10^−21 |
| CABLES1    | −2.5802 | 1.06×10^−22 | 2.30×10^−21 |
| SCARF1     | −2.57314| 3.55×10^−34 | 2.18×10^−32 |
| ENG        | −2.55959| 2.48×10^−20 | 1.32×10^−18 |
| RNASE4     | −2.5375 | 4.20×10^−28 | 1.54×10^−26 |
| CYBRD1     | −2.52939| 4.89×10^−27 | 1.65×10^−25 |

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| Gene symbol | Log_{2} FC | p-value     | FDR        |
|------------|------------|-------------|------------|
| GMFG       | -2.52643   | 3.54×10^{-22} | 7.28×10^{-21} |
| CITED2     | -2.51951   | 4.01×10^{-28} | 1.48×10^{-26} |
| TSPAN4     | -2.4885    | 1.28×10^{-25} | 3.82×10^{-24} |
| TNFSF13    | -2.48415   | 2.62×10^{-34} | 1.64×10^{-32} |
| CALCRL     | -2.4676    | 3.28×10^{-24} | 8.39×10^{-23} |
| AK1        | -2.45049   | 1.71×10^{-42} | 1.76×10^{-39} |
| ATP11A     | -2.42464   | 1.01×10^{-24} | 3.74×10^{-21} |
| CITED2     | -2.41951   | 4.01×10^{-28} | 1.48×10^{-26} |
| TSPAN4     | -2.4885    | 1.28×10^{-25} | 3.82×10^{-24} |
| TNFSF13    | -2.48415   | 2.62×10^{-34} | 1.64×10^{-32} |
| CALCRL     | -2.4676    | 3.28×10^{-24} | 8.39×10^{-23} |
| AK1        | -2.45049   | 1.71×10^{-42} | 1.76×10^{-39} |
| ATP11A     | -2.42464   | 1.01×10^{-24} | 3.74×10^{-21} |
| CITED2     | -2.41951   | 4.01×10^{-28} | 1.48×10^{-26} |
| TSPAN4     | -2.4885    | 1.28×10^{-25} | 3.82×10^{-24} |
| TNFSF13    | -2.48415   | 2.62×10^{-34} | 1.64×10^{-32} |
| CALCRL     | -2.4676    | 3.28×10^{-24} | 8.39×10^{-23} |
| AK1        | -2.45049   | 1.71×10^{-42} | 1.76×10^{-39} |
| ATP11A     | -2.42464   | 1.01×10^{-24} | 3.74×10^{-21} |
| Gene symbol | Log FC  | p-value   | FDR    |
|-------------|---------|-----------|--------|
| UNC13B      | -2.15658| 2×10⁻¹⁰⁻²⁶ | 1.60×10⁻²² |
| GPR4        | -2.08624| 2.52×10⁻¹⁰⁻²⁵ | 7.27×10⁻²⁴ |
| CD83        | -2.13621| 2.53×10⁻¹⁰⁻²³ | 5.81×10⁻²² |
| MOSC2       | -2.13581| 5.33×10⁻¹⁰⁻²⁸ | 1.93×10⁻²⁶ |
| RBMS2       | -2.12845| 4.40×10⁻¹⁰⁻³² | 1.91×10⁻²⁸ |
| PRKCE       | -2.11187| 2.70×10⁻¹⁰⁻²³ | 6.18×10⁻²² |
| FAM167B     | -2.0907 | 9.79×10⁻¹⁰⁻²⁸ | 3.46×10⁻²⁶ |
| GPD1L       | -2.0815 | 3.39×10⁻¹⁰⁻²⁶ | 1.04×10⁻²⁴ |
| SECISBP2L   | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| RBPMS       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| PRKCE       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| UNC13B      | -2.15658| 2×10⁻¹⁰⁻²⁶ | 1.60×10⁻²² |
| GPR4        | -2.08624| 2.52×10⁻¹⁰⁻²⁵ | 7.27×10⁻²⁴ |
| CD83        | -2.13621| 2.53×10⁻¹⁰⁻²³ | 5.81×10⁻²² |
| MOSC2       | -2.13581| 5.33×10⁻¹⁰⁻²⁸ | 1.93×10⁻²⁶ |
| RBMS2       | -2.12845| 4.40×10⁻¹⁰⁻³² | 1.91×10⁻²⁸ |
| PRKCE       | -2.11187| 2.70×10⁻¹⁰⁻²³ | 6.18×10⁻²² |
| FAM167B     | -2.0907 | 9.79×10⁻¹⁰⁻²⁸ | 3.46×10⁻²⁶ |
| GPD1L       | -2.0815 | 3.39×10⁻¹⁰⁻²⁶ | 1.04×10⁻²⁴ |
| SECISBP2L   | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| RBPMS       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| PRKCE       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| UNC13B      | -2.15658| 2×10⁻¹⁰⁻²⁶ | 1.60×10⁻²² |
| GPR4        | -2.08624| 2.52×10⁻¹⁰⁻²⁵ | 7.27×10⁻²⁴ |
| CD83        | -2.13621| 2.53×10⁻¹⁰⁻²³ | 5.81×10⁻²² |
| MOSC2       | -2.13581| 5.33×10⁻¹⁰⁻²⁸ | 1.93×10⁻²⁶ |
| RBMS2       | -2.12845| 4.40×10⁻¹⁰⁻³² | 1.91×10⁻²⁸ |
| PRKCE       | -2.11187| 2.70×10⁻¹⁰⁻²³ | 6.18×10⁻²² |
| FAM167B     | -2.0907 | 9.79×10⁻¹⁰⁻²⁸ | 3.46×10⁻²⁶ |
| GPD1L       | -2.0815 | 3.39×10⁻¹⁰⁻²⁶ | 1.04×10⁻²⁴ |
| SECISBP2L   | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| RBPMS       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| PRKCE       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| UNC13B      | -2.15658| 2×10⁻¹⁰⁻²⁶ | 1.60×10⁻²² |
| GPR4        | -2.08624| 2.52×10⁻¹⁰⁻²⁵ | 7.27×10⁻²⁴ |
| CD83        | -2.13621| 2.53×10⁻¹⁰⁻²³ | 5.81×10⁻²² |
| MOSC2       | -2.13581| 5.33×10⁻¹⁰⁻²⁸ | 1.93×10⁻²⁶ |
| RBMS2       | -2.12845| 4.40×10⁻¹⁰⁻³² | 1.91×10⁻²⁸ |
| PRKCE       | -2.11187| 2.70×10⁻¹⁰⁻²³ | 6.18×10⁻²² |
| FAM167B     | -2.0907 | 9.79×10⁻¹⁰⁻²⁸ | 3.46×10⁻²⁶ |
| GPD1L       | -2.0815 | 3.39×10⁻¹⁰⁻²⁶ | 1.04×10⁻²⁴ |
| SECISBP2L   | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| RBPMS       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| PRKCE       | -2.07935| 1.67×10⁻¹⁰⁻²³ | 3.57×10⁻²³ |
| Gene symbol | Log 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       | -1.71992 | 1.42×10⁻³⁴ | 3.04×10⁻³¹ |
| SLC27A3     | -1.71357 | 1.71×10⁻²² | 3.62×10⁻²¹ |
| PXMP4       | -1.71915 | 1.71×10⁻²² | 3.62×10⁻²¹ |
| LATS2       | -1.71534 | 1.42×10⁻²² | 3.04×10⁻³¹ |
| SLCL27A3    | -1.71357 | 1.71×10⁻²² | 3.62×10⁻²¹ |
| C7orf23     | -1.70414 | 1.95×10⁻⁴⁵ | 9.96×10⁻⁴³ |
| ADCY9       | -1.70113 | 1.86×10⁻³⁸ | 9.96×10⁻³⁶ |
| CASKIN2     | -1.70048 | 2.59×10⁻²² | 4.02×10⁻²¹ |
| UBL3        | -1.6965  | 3.62×10⁻²³ | 7.56×10⁻²¹ |
| PLEKH02     | -1.69433 | 3.80×10⁻²³ | 8.63×10⁻²² |
| PNPLA6      | -1.6739  | 8.43×10⁻³⁰ | 4.20×10⁻²⁹ |
| ST6GALNAC6  | -1.6565  | 1.25×10⁻³³ | 2.59×10⁻³¹ |
| DOK4        | -1.63599 | 1.49×10⁻²³ | 3.54×10⁻²² |
| RARA        | -1.6346  | 4.72×10⁻²³ | 9.96×10⁻²¹ |
| C1orf53     | -1.6321  | 3.91×10⁻²³ | 1.33×10⁻²¹ |
| PHF17       | -1.62738 | 1.07×10⁻²⁵ | 3.21×10⁻²⁴ |
| VAMP2       | -1.61336 | 6.49×10⁻³² | 3.31×10⁻³⁰ |
| C5orf32     | -1.58705 | 3.24×10⁻³² | 1.32×10⁻³⁰ |
| ARRB2       | -1.58449 | 9.32×10⁻³² | 3.30×10⁻²⁶ |
| AKAP13      | -1.57621 | 2.28×10⁻³⁰ | 1.27×10⁻²⁹ |
| C1orf19B    | -1.57187 | 6.00×10⁻³² | 3.06×10⁻³⁰ |
| SIDT2       | -1.56552 | 4.55×10⁻²⁶ | 1.39×10⁻²⁴ |
| SLC35A1     | -1.52742 | 2.71×10⁻²⁵ | 7.74×10⁻²⁴ |
| TAP1        | -1.50832 | 5.45×10⁻³² | 2.80×10⁻²⁰ |
| C1orf19B    | -1.50273 | 4.62×10⁻²⁴ | 1.41×10⁻²² |
| KIF1C       | -1.49667 | 3.00×10⁻²³ | 6.85×10⁻²² |
| MAP3K3      | -1.49287 | 1.47×10⁻²⁸ | 5.66×10⁻²⁶ |
| SH3D19      | -1.48881 | 1.09×10⁻²ⁱ | 2.61×10⁻²⁰ |
| CARD8       | -1.48471 | 1.78×10⁻²² | 3.75×10⁻²¹ |
| ARHGEF3     | -1.48222 | 4.88×10⁻²⁵ | 1.35×10⁻²³ |
| QSOX1       | -1.47038 | 2.94×10⁻²⁰ | 6.06×10⁻¹⁹ |
| RILPL2      | -1.41977 | 1.58×10⁻²⁴ | 4.17×10⁻²³ |
| RAB88       | -1.41917 | 5.62×10⁻²³ | 1.25×10⁻²¹ |
| B1D         | -1.41871 | 2.49×10⁻²⁷ | 5.16×10⁻²⁵ |
| C1orf32     | -1.41146 | 8.63×10⁻²¹ | 1.89×10⁻²⁰ |
| PPM1M       | -1.40925 | 1.13×10⁻²² | 2.43×10⁻²¹ |
| HSD17B1     | -1.39022 | 4.87×10⁻³⁰ | 3.53×10⁻²⁸ |
| 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^{-32} | 2.53×10^{-31} |
| 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^{-23} | 3.15×10^{-22} |
| SDCBP       | -1.27078   | 1.95×10^{-23} | 4.0×10^{-22} |
| GNAI2       | -1.24954   | 2.09×10^{-28} | 6.55×10^{-27} |
| CD81        | -1.21589   | 6.65×10^{-28} | 2.01×10^{-27} |
| INPP5K      | -1.14701   | 2.93×10^{-28} | 1.10×10^{-26} |
| COL4A3BP    | -1.14432   | 1.75×10^{-29} | 5.05×10^{-28} |
| SEC22C      | -1.13898   | 1.14×10^{-29} | 3.68×10^{-28} |
| SNX2        | -1.02367   | 9.40×10^{-29} | 2.53×10^{-28} |
| SACM1L      | -1.00516   | 4.74×10^{-29} | 1.20×10^{-28} |
| ZFYVE20     | -0.93822   | 7.39×10^{-29} | 1.82×10^{-28} |
| GORASP1     | -0.88378   | 6.42×10^{-29} | 1.75×10^{-28} |

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           | FGF4, FGFR4, CHAF1A, HSD17B4, TMEM669, PLK1, ROBO4, CBLC, GPR116, NAA50, ARHGAPE6, MC66, DTYMK, PTPRM, RPS6KA2, CHRNAS5, CYR1, WDR62, AS1F1, GNGT1, TB1T2M, GSTM5, ANLN, FLAD1, DNAB11, MUSTN1, C10orf32, LRRCD3, ECT2, PPP1R14B, ALDH2, CRY2, AR, RNASE4, KRT74, FOXE1, BRCA1, SOX17, C5AR1, AKFB4, POC1A, C1orf162, RNASE1, SLCT7A5, FAM72A, CBX7, PGM5, PCDH12, SSX2IP, TM6SF1, PALM2-APK2, ACOX1, PITX2, PSAT1, FZD4, DSP, UTRN, KIF22, CENPE, TMEM189, FAM72D, TMEM132A, TERT, Dlx6, KIFIC, STX12, GORASP1, ATAD5, TK1, LRRK2, GGC, KIF11, LMB1, SLC25A10, ZC3H8, TRPV2, POL2R2, CALCRL, MMNR1, CD34, MMP1, CDC25A, RAB8B |
| BRCA1 | 2.0335    | Up      | 82           | BLM1, CEL5B, ACACB, CD302, DUSP9, PAPPC2, GORASP1, LAMP3, MCM4, GYLT1B, FLAD1, TNS4, HSD17B4, STRA6, FAM83D, DAPK2, MARCO, EFNA4, PDE1B, PSRC1, COL4A3, ASAH1, TIMM8A, ERCC6L, CBLC, SORBS1, HOXP, CCDC58, CLEC14A, PLEKHO2, BTBD9, PALB2, KIF4A, SSX2IP, SPOCK2, EDRNRB, ADAMTS14, PTH1R, GGCT, UBE2T, HILLS, ABC6, ADCY9, NEK2, PHACT1, TP1, TROAP, ABCA12, TMPS5S11F, CENPK, PRPF19, ATP11A, TOP2A, SNRA1, SUV39H2, DSP, SACM1L, HDAC2, ELTD1, TPX2, B4GALT4, TXN, GCOM1, PID1, HBB, MYO19, AATK, NLR4, BLM, SH3BP5, GIMAP6, GLIPR2, GNAQ, MELK, MND1, SKA3, ADAMTS8, RPS6KA2, CHAF1A, ITGA10, CALCCO1 |
| NFATC2 | -2.5949   | Down    | 75           | IGSF9, SH3BP5, KRT16, PTLH1, PTPN21, CARD8, PSMD12, MELK, GPHBP1, RAD51AP2, DUSP1, CBL, GPR49, RGS4, VPS3, DUSP2, CBL, GPR49, RGS4, VPS3, CBL, GPR49, RGS4, VPS3 |

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