Revealing IncRNA Biomarkers Related to Chronic Obstructive Pulmonary Disease Based on Bioinformatics

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Background: Chronic obstructive pulmonary disease (COPD) is a common chronic disease of the respiratory tract, with high prevalence, high disability, and poor prognosis. However, the molecular mechanism of COPD needs to be further revealed.

Methods: We obtained the gene expression profile and miRNA expression profile of COPD patients from Gene Expression Omnibus (GEO) database, and the differentially expressed genes (DEGs) and differentially expressed miRNAs (DEmis) in COPD were identified. Subsequently, the COPD-related ceRNA network was constructed based on the interaction between lncRNA, miRNA, and mRNA using the lncACTdb database. Finally, the Cytoscape software was used to analyze the network topology and COPD-related lncRNAs.

Results: Firstly, the 519 DEGs and 17 DEmis were identified from COPD GEO datasets. GO enrichment showed that leukocyte chemotaxis, cell chemotaxis, and myeloid leukocyte migration were upregulated, and muscle and membrane repolarization-related biological progress were downregulated in COPD. KEGG pathway enrichment shows that the p53 pathway was upregulated in COPD. Hallmark enrichment showed that chronic neutrophil inflammation was a sign of the pathogenesis of COPD. Next, a ceRNA network including 93 DEGs, 2 DEmi, 463 lncRNAs, and 1157 DEG-lncRNA, DEmi-lncRNA, and DEmi-DEG interactions were obtained. The hub-lncRNA (the network is ranked in the top 10) as the core marker of COPD, including SNHG12, SLFLN1-AS1, KCNQ1OT1, XIST, EAF1-AS1, FOXD2-AS1, NORAD, PINK1-AS and RP11-69E11.4. And the cytoHubba analysis identified ATM, SMAD7 and HIF1A as hub genes of ceRNA network.

Conclusion: This study provides a landscape of ceRNA network of COPD, which help to reveal the underlying pathophysiological mechanisms of COPD and shed light on novel therapeutic strategies for COPD.

Keywords: chronic obstructive pulmonary disease, lncRNA, miRNA, bioinformatics

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic bronchitis or emphysema hallmark by chronic respiratory symptoms and airflow restriction, which can further develop into common chronic diseases of pulmonary heart disease and respiratory failure. The prevalence of COPD is increasingly worldwide, which become a great individual and society burden. As the COPD is often punctuated by rhinoviruses (RVs), the acute exacerbations frequently lead to morbidity and mortality of these patients. Although smoking and aging are the main causes of COPD, however, the pathological mechanism of COPD remains limited. The underlying pathophysiological mechanism is urgent for developing new therapies for COPD.

The dysregulation of mRNA and miRNA expression was also observed in COPD. A microarray of epithelium from COPD survey the TLR family gene expression and revealed that TLR5 is essential for the activation of innate immune responses in COPD. The aging-related genes were also differently expressed in COPD. The distinct miRNA profile was also observed in COPD. Moreover, the study showed that MicroRNA-218 regulated the overproduction of MUC5AC
and inflammation of COPD by targeting TNFR1-mediated NF-κB pathway. Recently, microRNA-21 was reported to mediate COPD pathogenesis by regulating SATB1/S100A9/NF-κB axis.\(^8\)

Emerging studies showed that the genetic factors are also important determinants of COPD. Long non-coding RNA (lncRNA) is a type of single-stranded non-coding RNA with the length of longer than 200 nucleotides that participate in various biological processes by manipulating gene expression.\(^9\) Recently, lncRNAs have been documented to play a key role in diverse biological functions and be involved in various disease including COPD and airway disease.\(^10\) A recent study revealed the significant different lncRNA expression profiles in smokers with or without COPD. Moreover, lncRNAs was reported to perform essential functions in the progression of COPD. lncRNA TUG1 was reported to reduce proliferation in COPD by inducing -β.\(^11\) Research by Li et al showed that lncRNA MIR155HG regulates/macrophage polarization in COPD.\(^12\) Zheng et al found that lncRNA COPDA1 promotes the proliferation of human bronchial smooth muscle cells in COPD.\(^13\) As the key regulator of miRNA, lncRNA was reported to regulate the COPD progression by targeting miRNA and mRNA.\(^14,15\) However, the landscape of COPD ceRNA network is limited.

In this study, we performed differential analysis of genes and miRNA expression profiles in COPD patients to obtain COPD-related genes and miRNAs, and constructed a COPD ceRNA network based on the interaction between genes, miRNAs and lncRNAs in the lncACTdb database. And then Cytoscape was used to perform topological analysis on the ceRNA network, and we obtained 10 lncRNAs as hub nodes, which were expected to become potential therapeutic targets for COPD.

**Materials and Methods**

**Data Collection**

We searched the mRNA and miRNA expression profiles of patients with COPD in the Gene Expression Omnibus (GEO) database based on the keywords “COPD”, “Home sapiens”, “mRNA profiles” and “miRNA profiles”. A total of 16 items were identified. Finally, after screening for the presence or absence of normal samples and the source of the samples, 148 samples from the four studies were used for subsequent analysis. The detailed information of the data set is shown in **Table 1**.

**Data Preprocessing and Differential Expression Analysis**

The original data was downloaded and the R package “limma” was used for analysis. Firstly, the original data was normalized (log2), and then differently expressed genes between COPD and normal samples were analyzed (lmFit and eBay functions) with the threshold used is fold change (log2) cutoff of 1 and p value cutoff of 0.05. Each data set was analyzed separately. Volcano maps and gene expression heat maps were performed by R package “ggplot2 and pheatmap”.

**PPI Network Analysis**

The protein–protein interaction (PPI) network can help us identify the key genes for the occurrence and development of COPD from the level of interaction. Get the PPI information of DEGs from the Search tool for the retrieval of Interacting Genes (STRING) database (http://www.string-db.org).\(^10\) Then, Cytoscape v3.7.0 software was used to analyze the topology of the PPI network in COPD, and the PPI network was constructed.

**Table 1** Datasets

| Accession | Experiment | Platform | COPD | Normal | Mrna/microRNA |
|-----------|------------|----------|------|--------|---------------|
| GSE38974  | Array      | GPL7723  | 19   | 8      | microRNA      |
| GSE38974  | Array      | GPL4133  | 23   | 9      | mRNA          |
| GSE103174 | Array      | GPL13667 | 37   | 16     | mRNA          |
| GSE135188 | RNA-seq    | GPL21290 | 18   | 18     | mRNA          |
GO/KEGG Enrichment Analysis
In order to study the biological functions of DEG, the R package ClusterProfiler was used to analyze and visualize the functional map of DEGs (Gene Ontology (GO) annotation and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway) and the annotative R package (org.Hs.eg.db) was selected as background. P value <0.05 is statistically significant.

Hallmark Feature Enrichment
In order to explore the enrichment of DEG in the biological state and process, the Hallmark gene set was downloaded from the MsigDB database, and the gene set of each pathway in the hallmark and the overlap of DEG were calculated by hypergeometric analysis. The enrichment threshold is P value <0.05.

Figure 1 The DEG in COPD samples and normal samples. (A) The volcano plots of DEGs in COPD using GSE38974 dataset. (B) The volcano plots of DEGs in COPD using GSE103174 dataset. (C) The volcano plots of DEGs in COPD using GSE135188 datasets. (D) The heat maps of DEGs in COPD samples and normal samples using GSE38974. (E) The heat maps of DEGs in COPD samples and normal samples in the GSE103174. (F) The heat maps of DEGs in COPD samples and normal samples in the GSE135188 datasets. (G) The network of DEGs in COPD.
Construction of ceRNA Network
The LncACTdb 2.0 (http://www.bio-bigdata.net/LncACTdb/) database contained the ceRNA interaction relationships from multiple documents. The DEGs and DEmis were submitted to the database, and then the related lncRNA, the interactions between DEGs and lncRNA, DEmi and lncRNA, and DEG and DEmiRNA were obtained. According to the ceRNA theory, the selected DEmi and DEG, DEmi and lncRNA, and DEG and IncRNA were integrated and interacted with each other, and the DEmi-DEG-lncRNA ceRNA network was constructed using Cytoscape v3.7.0 software.

Statistical Analysis
All data were analyzed using R (v 4.0.3). The different expression analysis was performed using R “limma” packages. Student’s t-tests were used to calculate P-values by t.test function. The heatmaps were generated by pheatmap R package (v 1.0.12).

Result
DEG and DEmi Related to COPD Was Screened
Firstly, the 519 DEGs from the mRNA expression between COPD samples and normal samples from three GEO datasets were obtained with a threshold of p value <0.05 and |logFC|>1. Among them, 233 up-regulated DEGs, 240 down-regulated DEGs were identified in the data set GSE38974; 10 up-regulated DEGs and 12 down-regulated DEGs were identified in the data set GSE103174, and 16 up-regulated DEGs and 31 down-regulated DEGs were identified in the data set GSE135188. The DEGs volcano map of the above three datasets are shown in Figure 1A–C, and the heatmap is shown in Figure 1D–F. In the DEG expression heatmap, there was significant heterogeneity between the expression of DEGs in COPD samples and normal samples. Next, we use all 519 DEGs to construct a PPI network in Figure 1G. In the constructed PPI-DEG network, there were a total of 139 DEGs and 166 interaction relationships. Among them, UBD, H2AFX, BAG3, and CDKN1A were key genes in the network of COPD. Zhang et al determined the modular gene markers containing H2AFX by analyzing the protein interaction network as a marker for distinguishing COPD and NSCLC.16 Sun et al identified 40 potential COPD-related genes through bioinformatics analysis and found that HIF1A, CDKN1A, BAG3, ERBB2, and ATG16L1 may affect the development of COPD by regulating autophagy.17

Figure 2 The differential microRNAs (DEmi) in COPD samples and normal samples. (A) The volcano plots of DEmi obtained from the data set GSE38974 with P <0.05 and |log2 (FC)| > 1. The small diamond presents the microRNAs. (B) The heat map of DEmi of COPD samples and normal samples in the data set GSE38974.
We next selected 17 DEmis from the data set GSE38974 by using the same threshold as that used to obtain DEGs, including 11 up-regulated DEmis and 6 down-regulated DEmis. The volcano map and heatmap of DEmis are shown in Figure 2A and B, respectively.

**Functional Enrichment of DEG in COPD**

In order to explore the biological significance of COPD features, all DEGs from GSE38974, GSE103174 and GSE135188 were used for GO/KEGG analysis using the Hallmark gene sets in MSigDB. As shown in Figure 3A, GO enrichment showed that leukocyte chemotaxis, cell chemotaxis and myeloid leukocyte migration were upregulated, and muscle and membrane repolarization-related biological progresses were downregulated in COPD. The cytokine receptor CXCR2 antagonist (MK-7123) reduced the chemotaxis of neutrophils, which may alleviate the airway inflammation of COPD, and aerobic training combined with respiratory muscle stretching improved the functional exercise capacity of COPD patients and reduced dyspnea. In Figure 3B, KEGG pathway enrichment shows that p53 pathway was upregulated in COPD. The p53 signaling pathway polymorphism was associated with changes in emphysema in COPD patients, and compared with non-smokers, healthy smokers and COPD smokers due to the apoptosis of active pulmonary capillary endothelial cells, the level of circulating endothelial cells increased. Dinesh et al also revealed the

![Figure 3](https://doi.org/10.2147/COPD.S354634)
increased apoptotic cell death in airway epithelial cells in COPD.\textsuperscript{10} We also found in the Hallmark enrichment results of Figure 3C and D that chronic neutrophil inflammation was a sign of the pathogenesis of COPD, which persists after smoking cessation.\textsuperscript{22} And COPD patients may be particularly vulnerable to hypoxia-induced autonomic disorders.\textsuperscript{23}

\textbf{IncRNA Marker is Screened Based on DEG and DEmi}

We obtained the RNA interaction relationship from the database lncACTdb 2.0, and constructed the interaction relationship network containing 519 DEGs and 17 DEmis. The ceRNA network we obtained (Figure 4) contains 93 DEGs, 2 DEmi, 463 lncRNAs, and 1157 DEG-lncRNA, DEmi-lncRNA, and DEmi-DEG interactions. The network node degree is shown in Table 2. In the constructed ceRNA network, we selected hub-lncRNA (the network is ranked in the top 10) as the core marker of COPD, including SNHG12, SLFNL1-AS1, KCNQ1OT1, XIST, EAF1-AS1, FOXD2-AS1, NORAD, PINK1-AS and RP11-69E11.4. Next, basing on the cytoHubba analysis of cytoscape, ATM, SMAD7 and HIF1A were identified as hub genes in this network and are used for the treatment of COPD in the future (Figure 5).

\textbf{Discussion}

COPD is a chronic progressive inflammatory disease with poor prognosis and low long-term survival rate.\textsuperscript{24} Pulmonary rehabilitation is traditionally recommended for patients with moderate to severe COPD. Although pulmonary rehabilitation, bronchodilators and anti-inflammatory agents provides the greatest improvement in dyspnea, exercise tolerance, and health-related quality of life,\textsuperscript{25} it is very difficult to change physical activity and with poor outcome.\textsuperscript{26} Therefore, COPD is a major heterogeneous disease and one of the world’s leading causes of death, and it is urgent for diagnostic and prognostic biomarkers for COPD.
Table 2 The Network Node Degree

| Gene   | RNA   | Up/Down | Degree |
|--------|-------|---------|--------|
| AADAC  | mRNA  | Down    | 0      |
| ABCG2  | mRNA  | Down    | 17     |
| AC002117.1 | IncRNA | Plane   | 1      |
| AC002467.7 | IncRNA | Plane   | 1      |
| AC003104.1 | IncRNA | Plane   | 4      |
| AC003991.3 | IncRNA | Plane   | 3      |
| AC004069.2 | IncRNA | Plane   | 1      |
| AC004448.5 | IncRNA | Plane   | 1      |
| AC005154.6 | IncRNA | Plane   | 6      |
| AC005532.5 | IncRNA | Plane   | 2      |
| AC007228.9 | IncRNA | Plane   | 1      |
| AC007292.6 | IncRNA | Plane   | 1      |
| AC008079.10 | IncRNA | Plane  | 2      |
| AC008697.1 | IncRNA | Plane   | 1      |
| AC009133.12 | IncRNA | Plane  | 2      |
| AC009948.5 | IncRNA | Plane   | 5      |
| AC010136.2 | IncRNA | Plane   | 1      |
| AC010226.4 | IncRNA | Plane   | 1      |
| AC012123.1 | IncRNA | Plane   | 1      |
| AC015849.16 | IncRNA | Plane  | 2      |
| AC015933.2 | IncRNA | Plane   | 1      |
| AC016747.3 | IncRNA | Plane   | 1      |
| AC017060.1 | IncRNA | Plane   | 1      |
| AC017101.10 | IncRNA | Plane  | 5      |
| AC018890.6 | IncRNA | Plane   | 2      |
| AC023347.1 | IncRNA | Plane   | 1      |
| AC034220.3 | IncRNA | Plane   | 1      |
| AC058791.1 | IncRNA | Plane   | 2      |
| AC069363.1 | IncRNA | Plane   | 2      |
| AC073254.1 | IncRNA | Plane   | 1      |
| AC073641.2 | IncRNA | Plane   | 3      |
| AC074117.10 | IncRNA | Plane  | 1      |
| AC074286.1 | IncRNA | Plane   | 3      |
| AC074366.3 | IncRNA | Plane   | 2      |
| AC084219.4 | IncRNA | Plane   | 2      |
| AC104134.2 | IncRNA | Plane   | 2      |
| AC107081.5 | IncRNA | Plane   | 2      |
| AC108142.1 | IncRNA | Plane   | 1      |
| AC116366.5 | IncRNA | Plane   | 1      |
| AC139100.4 | IncRNA | Plane   | 1      |
| AC141928.1 | IncRNA | Plane   | 1      |
| ACAN   | mRNA  | Down    | 0      |
| ACSL5  | mRNA  | Up      | 0      |
| ACTA2  | mRNA  | Down    | 12     |
| ACTBL2 | mRNA  | Down    | 0      |
| ACTG2  | mRNA  | Down    | 0      |
| ACTN3  | mRNA  | Down    | 0      |
| ADAMTS4| mRNA  | Up      | 1      |

(Continued)
Table 2 (Continued).

| Gene         | RNA     | Up/down | Degree |
|--------------|---------|---------|--------|
| ADH1A        | mRNA    | Down    | 0      |
| ADH1C        | mRNA    | Down    | 0      |
| ADORA2A-AS1  | lncRNA  | Plane   | 1      |
| AF127936.9   | lncRNA  | Plane   | 1      |
| AF146191.4   | lncRNA  | Plane   | 1      |
| AGBL1        | mRNA    | Down    | 0      |
| AGBL2        | mRNA    | Down    | 0      |
| AGER         | mRNA    | Down    | 0      |
| AGTR2        | mRNA    | Up      | 0      |
| AK2P2        | mRNA    | Up      | 0      |
| AKAP14       | mRNA    | Down    | 0      |
| AKIRIN1      | mRNA    | Up      | 0      |
| AL133243.1   | lncRNA  | Plane   | 1      |
| ALAS2        | mRNA    | Up      | 0      |
| ALG6         | mRNA    | Down    | 0      |
| ALKBH3-AS1   | lncRNA  | Plane   | 1      |
| ALMS1-IT1    | lncRNA  | Plane   | 1      |
| ALOX12-AS1   | lncRNA  | Plane   | 2      |
| AMOTL2       | mRNA    | Down    | 0      |
| ANKMY2       | mRNA    | Down    | 0      |
| ANKRD22      | mRNA    | Up      | 0      |
| ANO8         | mRNA    | Up      | 0      |
| ANXA2P3      | mRNA    | Down    | 0      |
| ANXA5        | mRNA    | Down    | 0      |
| ANXA6        | mRNA    | Up      | 0      |
| AP001258.4   | lncRNA  | Plane   | 1      |
| AP006621.8   | lncRNA  | Plane   | 1      |
| APAF1        | mRNA    | Up      | 23     |
| APOBEC3A     | mRNA    | Up      | 0      |
| APOBEC3C     | mRNA    | Up      | 0      |
| ARHGAP26     | mRNA    | Up      | 2      |
| ARL4C        | mRNA    | Up      | 2      |
| ARNTL2       | mRNA    | Up      | 0      |
| ART4         | mRNA    | Down    | 0      |
| ASPHDI       | mRNA    | Up      | 0      |
| ASPN         | mRNA    | Down    | 0      |
| ATF3         | mRNA    | Up      | 5      |
| ATM          | mRNA    | Up      | 72     |
| ATP1A2       | mRNA    | Down    | 0      |
| ATP1B2       | mRNA    | Down    | 0      |
| AXUD1        | mRNA    | Up      | 0      |
| BACE1-AS     | lncRNA  | Plane   | 1      |
| BAG3         | mRNA    | Up      | 1      |
| BAI3         | mRNA    | Down    | 0      |
| BAIAP2-AS1   | lncRNA  | Plane   | 1      |
| BAX          | mRNA    | Up      | 22     |
| BCDIN3D-AS1  | lncRNA  | Plane   | 1      |
| BCHE         | mRNA    | Down    | 0      |
| BCL2A1       | mRNA    | Up      | 0      |
| BDKRBI       | mRNA    | Up      | 0      |

(Continued)
Table 2 (Continued).

| Gene            | RNA     | Up/Down | Degree |
|-----------------|---------|---------|--------|
| BPIFA1          | mRNA    | Down    | 0      |
| BVES-AS1        | lncRNA  | Plane   | 1      |
| C10orf116       | mRNA    | Down    | 0      |
| C10orf28        | mRNA    | Down    | 0      |
| C11orf10        | mRNA    | Down    | 0      |
| C11orf88        | mRNA    | Down    | 0      |
| C13orf33        | mRNA    | Up      | 0      |
| C15orf48        | mRNA    | Up      | 0      |
| C17orf102       | lncRNA  | Plane   | 1      |
| C18orf32        | mRNA    | Up      | 0      |
| C1orf105        | mRNA    | Up      | 0      |
| C1orf132        | lncRNA  | Plane   | 1      |
| C1orf195        | lncRNA  | Plane   | 1      |
| C1QTNF5         | mRNA    | Down    | 0      |
| C1QTNF7         | mRNA    | Down    | 0      |
| C1RL-AS1        | lncRNA  | Plane   | 4      |
| C20orf46        | mRNA    | Down    | 0      |
| C20orf85        | mRNA    | Down    | 0      |
| C2orf40         | mRNA    | Down    | 0      |
| C2orf54         | mRNA    | Up      | 0      |
| C2orf83         | mRNA    | Down    | 0      |
| C4orf7          | mRNA    | Up      | 0      |
| C6              | mRNA    | Down    | 0      |
| C6orf124        | mRNA    | Up      | 0      |
| C6orf192        | mRNA    | Down    | 0      |
| C7orf23         | mRNA    | Down    | 0      |
| C9orf117        | mRNA    | Down    | 0      |
| C9orf171        | mRNA    | Down    | 0      |
| C9orf24         | mRNA    | Down    | 0      |
| CABP2           | mRNA    | Down    | 0      |
| CACNA1E         | mRNA    | Up      | 0      |
| CACNA1H         | mRNA    | Down    | 0      |
| CAPS            | mRNA    | Down    | 0      |
| CARD8-AS1       | lncRNA  | Plane   | 1      |
| CASC2           | lncRNA  | Plane   | 3      |
| CASC8           | lncRNA  | Plane   | 1      |
| CASK-AS1        | lncRNA  | Plane   | 1      |
| CASQ2           | mRNA    | Down    | 0      |
| CATIP-AS2       | lncRNA  | Plane   | 2      |
| CAVI            | mRNA    | Down    | 25     |
| CBX6            | mRNA    | Down    | 0      |
| CBY1            | mRNA    | Down    | 0      |
| CCDC103         | mRNA    | Down    | 0      |
| CCDC137         | mRNA    | Up      | 0      |
| CCDC17          | mRNA    | Down    | 0      |
| CCDC18-AS1      | lncRNA  | Plane   | 10     |
| CCDC48          | mRNA    | Down    | 0      |
| CCDC3           | mRNA    | Down    | 0      |
| CCDC37          | mRNA    | Down    | 0      |
| CCDC48          | mRNA    | Down    | 0      |

(Continued)
### Table 2 (Continued).

| Gene       | RNA  | Up/Down | Degree |
|------------|------|---------|--------|
| CCDC77     | mRNA | Down    | 0      |
| CCDC81     | mRNA | Down    | 0      |
| CCL19      | mRNA | Up      | 0      |
| CCL20      | mRNA | Up      | 4      |
| CCL8       | mRNA | Up      | 2      |
| CCR6       | mRNA | Up      | 0      |
| CD70       | mRNA | Up      | 0      |
| CD86       | mRNA | Down    | 4      |
| CDC42EP2   | mRNA | Up      | 0      |
| CDH3       | mRNA | Up      | 0      |
| CDKN1A     | mRNA | Up      | 70     |
| CDKN2B-AS1 | lncRNA| Plane | 1      |
| CES1       | mRNA | Down    | 0      |
| CFLAR-AS1  | lncRNA| Plane | 6      |
| CGB1       | mRNA | Down    | 0      |
| CH25H      | mRNA | Up      | 0      |
| CHI3L1     | mRNA | Up      | 0      |
| CHI3L2     | mRNA | Up      | 0      |
| CHIT1      | mRNA | Up      | 0      |
| CHMP4B     | mRNA | Up      | 0      |
| CHP2       | mRNA | Up      | 0      |
| CHST2      | mRNA | Up      | 0      |
| CKMT2-AS1  | lncRNA| Plane | 2      |
| CLC        | mRNA | Up      | 0      |
| CLEC4E     | mRNA | Up      | 0      |
| CLU        | mRNA | Down    | 20     |
| CMIP       | mRNA | Up      | 0      |
| CNN1       | mRNA | Down    | 0      |
| COL21A1    | mRNA | Down    | 3      |
| COL4A1     | mRNA | Down    | 41     |
| COL4A2-AS1 | lncRNA| Plane | 7      |
| COX10-AS1  | lncRNA| Plane | 3      |
| COX5A      | mRNA | Up      | 0      |
| CPA3       | mRNA | Down    | 0      |
| CPT2       | mRNA | Up      | 0      |
| CREB3L4    | mRNA | Down    | 0      |
| CRNDE      | lncRNA| Plane | 2      |
| CSF3       | mRNA | Up      | 0      |
| CTB-111H14.1| lncRNA| Plane | 1      |
| CTC-204F22.1| lncRNA| Plane | 6      |
| CTC-351M12.1| lncRNA| Plane | 7      |
| CTC-444N24.11| lncRNA| Plane | 1      |
| CTC-444N24.7| lncRNA| Plane | 4      |
| CTC-459F4.3| lncRNA| Plane | 1      |
| CTC-459F4.9| lncRNA| Plane | 2      |
| CTC-479C5.10| lncRNA| Plane | 4      |
| CTC-487M23.5| lncRNA| Plane | 5      |
| CTD-2047H16.3| lncRNA| Plane | 2      |
| CTD-2095E4.5| lncRNA| Plane | 5      |
| CTD-2292P10.4| lncRNA| Plane | 2      |

(Continued)
Table 2 (Continued).

| Gene          | RNA | Up/Down | Degree |
|---------------|-----|---------|--------|
| CTD-2337I7.1  | IncRNA | Plane | 1      |
| CTD-2369P2.5  | IncRNA | Plane | 1      |
| CTD-2410N18.4 | IncRNA | Plane | 3      |
| CTD-2510F5.4  | IncRNA | Plane | 3      |
| CTD-2517M22.14| IncRNA | Plane | 4      |
| CTD-2587H24.14| IncRNA | Plane | 2      |
| CTD-2619J13.14| IncRNA | Plane | 1      |
| CTD-2630F21.1 | IncRNA | Plane | 2      |
| CTD-3032J10.2 | IncRNA | Plane | 1      |
| CTD-3099C6.9  | IncRNA | Plane | 1      |
| CTD-3131K8.2  | IncRNA | Plane | 5      |
| CTGF          | mRNA  | Down   | 9      |
| CTSS          | mRNA  | Up     | 0      |
| CUL2          | mRNA  | Up     | 7      |
| CXCL13        | mRNA  | Up     | 0      |
| CYorf15B      | mRNA  | Up     | 0      |
| CYP1BI        | mRNA  | Up     | 3      |
| CYP3A4        | mRNA  | Down   | 3      |
| CYP3A7        | mRNA  | Down   | 0      |
| CYTOR         | IncRNA | Plane | 1      |
| DAWI          | mRNA  | Down   | 0      |
| DDC           | mRNA  | Down   | 1      |
| DDR2          | mRNA  | Down   | 0      |
| DENND4B       | mRNA  | Down   | 0      |
| DES           | mRNA  | Down   | 0      |
| DGUOK-AS1     | IncRNA | Plane | 3      |
| DHRS4-AS1     | IncRNA | Plane | 1      |
| DLEU2L        | IncRNA | Plane | 1      |
| DLST          | mRNA  | Up     | 0      |
| DLX6-AS1      | IncRNA | Plane | 5      |
| DNAJC5        | mRNA  | Up     | 0      |
| DNAJC7        | mRNA  | Up     | 0      |
| DNASEI1L3     | mRNA  | Down   | 0      |
| DOHH          | mRNA  | Up     | 10     |
| DPH6-AS1      | IncRNA | Plane | 2      |
| DPYD-AS1      | IncRNA | Plane | 5      |
| DSP15         | mRNA  | Down   | 0      |
| DSW3P2        | mRNA  | Up     | 4      |
| DYNC1H1       | mRNA  | Down   | 0      |
| DYNLRB2       | mRNA  | Down   | 0      |
| EAFI-AS1      | IncRNA | Plane | 12     |
| EBLN3P        | IncRNA | Plane | 8      |
| EEF1AI1P11    | mRNA  | Down   | 0      |
| EFHB          | mRNA  | Down   | 0      |
| EGFL7         | mRNA  | Down   | 0      |
| EIF1B         | mRNA  | Up     | 0      |
| EIF3j-AS1     | IncRNA | Plane | 2      |
| ELOA-AS1      | IncRNA | Plane | 3      |
| EMD           | mRNA  | Up     | 0      |
| EML2-AS1      | IncRNA | Plane | 1      |
Table 2 (Continued).

| Gene        | RNA   | Up/Down | Degree |
|-------------|-------|---------|--------|
| ENPP2       | mRNA  | Down    | 0      |
| ENPP4       | mRNA  | Down    | 0      |
| ENTPD1-AS1  | lncRNA| Plane   | 1      |
| ERF         | mRNA  | Up      | 0      |
| EXTL3-AS1   | lncRNA| Plane   | 3      |
| F8A1        | mRNA  | Down    | 0      |
| FAM162B     | mRNA  | Down    | 0      |
| FAM166B     | mRNA  | Up      | 0      |
| FAM183A     | mRNA  | Down    | 0      |
| FAM201A     | lncRNA| Plane   | 5      |
| FAM5C       | mRNA  | Down    | 0      |
| FAM95C      | lncRNA| Plane   | 1      |
| FAM96B      | mRNA  | Down    | 0      |
| FAT4        | mRNA  | Down    | 0      |
| FENDRR      | lncRNA| Plane   | 3      |
| FGFBP2      | mRNA  | Down    | 0      |
| FGG         | mRNA  | Up      | 2      |
| FHL1        | mRNA  | Down    | 0      |
| FIBIN       | mRNA  | Down    | 0      |
| FLIPI1      | mRNA  | Down    | 0      |
| FKBP10      | mRNA  | Up      | 0      |
| FLI21511    | mRNA  | Down    | 0      |
| FLJ34515    | mRNA  | Down    | 0      |
| FLJ37453    | lncRNA| Plane   | 3      |
| FLJ46284    | lncRNA| Plane   | 3      |
| FOLR1       | mRNA  | Down    | 0      |
| FOXD2-AS1   | lncRNA| Plane   | 11     |
| FSTL1       | mRNA  | Down    | 8      |
| FTX         | lncRNA| Plane   | 9      |
| FUS         | mRNA  | Up      | 0      |
| GABBR1      | mRNA  | Down    | 0      |
| GABRE       | mRNA  | Down    | 0      |
| GADD45B     | mRNA  | Up      | 0      |
| GAGE3       | mRNA  | Up      | 0      |
| GAS1        | mRNA  | Down    | 21     |
| GAS5        | lncRNA| Plane   | 2      |
| GBP6        | mRNA  | Down    | 0      |
| GDE1        | mRNA  | Up      | 0      |
| GDF10       | mRNA  | Down    | 0      |
| GDF15       | mRNA  | Up      | 0      |
| GFPT2       | mRNA  | Up      | 0      |
| GJB2        | mRNA  | Up      | 0      |
| GLT1D1      | mRNA  | Up      | 0      |
| GLT2SD2     | mRNA  | Down    | 0      |
| GLYCTK-AS1  | lncRNA| Plane   | 1      |
| GNA11       | mRNA  | Down    | 0      |
| GNG12-AS1   | lncRNA| Plane   | 2      |
| GNG13       | mRNA  | Down    | 2      |
| GPC3        | mRNA  | Down    | 1      |
| GPM6A       | mRNA  | Down    | 0      |

(Continued)
| Gene          | RNA     | Up/down | Degree |
|--------------|---------|---------|--------|
| GPR172A      | mRNA    | Up      | 0      |
| GPR177       | mRNA    | Up      | 0      |
| GRB14        | mRNA    | Down    | 0      |
| GRM8         | mRNA    | Down    | 0      |
| GSN          | mRNA    | Down    | 0      |
| GST2A        | mRNA    | Down    | 0      |
| GSTA5        | mRNA    | Down    | 0      |
| GSTM1        | mRNA    | Down    | 0      |
| GSTT1        | mRNA    | Down    | 0      |
| GUSBP11      | lncRNA  | Plane   | 1      |
| H19          | lncRNA  | Plane   | 4      |
| H2AFX        | mRNA    | Up      | 29     |
| HAGLR        | lncRNA  | Plane   | 3      |
| HAS1         | mRNA    | Up      | 0      |
| HCG18        | lncRNA  | Plane   | 3      |
| HCKT         | mRNA    | Down    | 0      |
| HELLPAR      | lncRNA  | Plane   | 1      |
| HIF1A        | mRNA    | Up      | 79     |
| HIRA         | mRNA    | Up      | 0      |
| HIST1H2AB    | mRNA    | Down    | 0      |
| HIST1H4B     | mRNA    | Down    | 0      |
| HK3          | mRNA    | Up      | 0      |
| HLA-U        | mRNA    | Up      | 0      |
| HMBOX1       | mRNA    | Down    | 3      |
| HMGB3L1      | mRNA    | Up      | 0      |
| HMOX1        | mRNA    | Up      | 5      |
| HNRNPA0      | mRNA    | Up      | 0      |
| HNRNPAB      | mRNA    | Up      | 0      |
| HORMAD2-AS1  | lncRNA  | Plane   | 1      |
| HOTAIRM1     | lncRNA  | Plane   | 1      |
| HOXA-AS2     | lncRNA  | Plane   | 4      |
| HOXA-AS3     | lncRNA  | Plane   | 3      |
| HOXA2        | mRNA    | Down    | 0      |
| HOXC-AS2     | lncRNA  | Plane   | 1      |
| HPR          | mRNA    | Up      | 0      |
| HRASL5S      | mRNA    | Up      | 0      |
| hsa-miR-105  | miRNA   | Up      | 0      |
| hsa-miR-10a  | miRNA   | Up      | 0      |
| hsa-miR-1274a| miRNA   | Up      | 0      |
| hsa-miR-144  | miRNA   | Up      | 0      |
| hsa-miR-148a | miRNA   | Up      | 0      |
| hsa-miR-223  | miRNA   | Up      | 0      |
| hsa-miR-25a  | miRNA   | Down    | 0      |
| hsa-miR-374a | miRNA   | Up      | 0      |
| hsa-miR-422a | miRNA   | Down    | 0      |
| hsa-miR-454  | miRNA   | Up      | 0      |
| hsa-miR-486-5p| miRNA  | Up      | 12     |
| hsa-miR-513a-5p| miRNA | Down    | 3      |
| hsa-miR-576-3p| miRNA  | Down    | 0      |
| hsa-miR-664  | miRNA   | Up      | 0      |

(Continued)
Table 2 (Continued).

| Gene          | RNA    | Up/Down | Degree |
|---------------|--------|---------|--------|
| hsa-miR-766   | miRNA  | Up      | 0      |
| hsa-miR-923   | miRNA  | Down    | 0      |
| hsa-miR-937   | miRNA  | Down    | 0      |
| HSPA2         | mRNA   | Down    | 0      |
| HSPB3         | mRNA   | Down    | 0      |
| HSPD1P6       | mRNA   | Up      | 0      |
| ID4           | mRNA   | Down    | 4      |
| IER3          | mRNA   | Up      | 0      |
| IFT1          | mRNA   | Down    | 4      |
| IFT20         | mRNA   | Up      | 0      |
| IGFBP7-AS1    | lncRNA | Plane   | 1      |
| IGHB          | mRNA   | Up      | 0      |
| IGSF6         | mRNA   | Up      | 0      |
| IL1B          | mRNA   | Up      | 1      |
| IL1R2         | mRNA   | Up      | 0      |
| IL20RB        | mRNA   | Up      | 0      |
| IL33          | mRNA   | Down    | 0      |
| IL6           | mRNA   | Up      | 31     |
| IL8           | mRNA   | Up      | 0      |
| INMT          | mRNA   | Down    | 0      |
| IPO9-AS1      | lncRNA | Plane   | 1      |
| IQCD          | mRNA   | Down    | 0      |
| IQGAP2        | mRNA   | Up      | 0      |
| IRX5          | mRNA   | Down    | 0      |
| ITGA7         | mRNA   | Down    | 4      |
| ITGA9-AS1     | lncRNA | Plane   | 4      |
| ITGB2         | mRNA   | Up      | 0      |
| ITLN2         | mRNA   | Down    | 0      |
| ITPKC         | mRNA   | Up      | 0      |
| JMJ D6        | mRNA   | Up      | 0      |
| JPX           | lncRNA | Plane   | 1      |
| JUNB          | mRNA   | Up      | 2      |
| KB-1208A12.3  | lncRNA | Plane   | 2      |
| KB-1517D11.4  | lncRNA | Plane   | 1      |
| KB-1572G7.2   | lncRNA | Plane   | 1      |
| KB-1615E4.2   | lncRNA | Plane   | 3      |
| KB-3188B.7    | lncRNA | Plane   | 3      |
| KC6           | lncRNA | Plane   | 1      |
| KCNA5         | mRNA   | Down    | 0      |
| KCNIP2-AS1    | lncRNA | Plane   | 1      |
| KCNQ1OT1      | lncRNA | Plane   | 16     |
| KDM4A-AS1     | lncRNA | Plane   | 10     |
| KIAA0644      | mRNA   | Down    | 0      |
| KIT           | mRNA   | Down    | 56     |
| KLK12         | mRNA   | Down    | 0      |
| KPNA6         | mRNA   | Down    | 0      |
| KRT17P3       | mRNA   | Up      | 0      |
| KRT4          | mRNA   | Down    | 0      |
| KRT7          | mRNA   | Up      | 6      |
| KRT7-AS       | lncRNA | Plane   | 2      |
Table 2 (Continued).

| Gene       | RNA      | Up/Down | Degree |
|------------|----------|---------|--------|
| L1TD1      | mRNA     | Down    | 0      |
| LA16c-358B7.3 | IncRNA | Plane   | 1      |
| LACTB2-AS1 | IncRNA   | Plane   | 1      |
| LAD1       | mRNA     | Up      | 0      |
| LDB2       | mRNA     | Down    | 0      |
| LEFTY2     | mRNA     | Down    | 0      |
| LILRB1     | mRNA     | Up      | 0      |
| LILRB2     | mRNA     | Up      | 0      |
| LIMD1-AS1  | IncRNA   | Plane   | 1      |
| LIMK1      | mRNA     | Up      | 24     |
| LIMS2      | mRNA     | Down    | 0      |
| LINC-PINT  | IncRNA   | Plane   | 6      |
| LINC00158  | IncRNA   | Plane   | 1      |
| LINC00304  | IncRNA   | Plane   | 1      |
| LINC00339  | IncRNA   | Plane   | 4      |
| LINC00461  | IncRNA   | Plane   | 1      |
| LINC00472  | IncRNA   | Plane   | 1      |
| LINC00511  | IncRNA   | Plane   | 3      |
| LINC00525  | IncRNA   | Plane   | 2      |
| LINC00630  | IncRNA   | Plane   | 1      |
| LINC00641  | IncRNA   | Plane   | 2      |
| LINC00645  | IncRNA   | Plane   | 1      |
| LINC00661  | IncRNA   | Plane   | 1      |
| LINC00664  | IncRNA   | Plane   | 1      |
| LINC00665  | IncRNA   | Plane   | 9      |
| LINC00667  | IncRNA   | Plane   | 3      |
| LINC00670  | IncRNA   | Plane   | 2      |
| LINC00707  | IncRNA   | Plane   | 1      |
| LINC00869  | IncRNA   | Plane   | 7      |
| LINC00893  | IncRNA   | Plane   | 2      |
| LINC00894  | IncRNA   | Plane   | 7      |
| LINC00907  | IncRNA   | Plane   | 1      |
| LINC00909  | IncRNA   | Plane   | 1      |
| LINC00910  | IncRNA   | Plane   | 1      |
| LINC00958  | IncRNA   | Plane   | 10     |
| LINC00960  | IncRNA   | Plane   | 2      |
| LINC00963  | IncRNA   | Plane   | 6      |
| LINC01085  | IncRNA   | Plane   | 1      |
| LINC01090  | IncRNA   | Plane   | 2      |
| LINC01116  | IncRNA   | Plane   | 1      |
| LINC01128  | IncRNA   | Plane   | 10     |
| LINC01134  | IncRNA   | Plane   | 2      |
| LINC01140  | IncRNA   | Plane   | 7      |
| LINC01184  | IncRNA   | Plane   | 1      |
| LINC01197  | IncRNA   | Plane   | 1      |
| LINC01257  | IncRNA   | Plane   | 1      |
| LINC01278  | IncRNA   | Plane   | 2      |
| LINC01358  | IncRNA   | Plane   | 2      |
| LINC01362  | IncRNA   | Plane   | 2      |
| LINC01521  | IncRNA   | Plane   | 1      |

(Continued)
| Gene                  | RNA  | Up/Down | Degree |
|-----------------------|------|---------|--------|
| LINC01569             | lncRNA | Plane  | 1      |
| LINC01578             | lncRNA | Plane  | 1      |
| LINC01605             | lncRNA | Plane  | 1      |
| LINC01619             | lncRNA | Plane  | 1      |
| LINC01783             | lncRNA | Plane  | 1      |
| LINC01934             | lncRNA | Plane  | 4      |
| LINC01965             | lncRNA | Plane  | 1      |
| LIXIL-AS1             | lncRNA | Plane  | 1      |
| LLNLR-268E12.1        | lncRNA | Plane  | 1      |
| LLNLR-470E3.1         | lncRNA | Plane  | 1      |
| LMCD1                 | mRNA  | Down   | 0      |
| LMNB1                 | mRNA  | Up     | 0      |
| LMNB2                 | mRNA  | Up     | 3      |
| LMOD1                 | mRNA  | Down   | 0      |
| LOC100128164          | mRNA  | Down   | 0      |
| LOC100128178          | mRNA  | Down   | 0      |
| LOC100128548          | mRNA  | Down   | 0      |
| LOC100128977          | mRNA  | Up     | 0      |
| LOC100131582          | mRNA  | Up     | 0      |
| LOC100132247          | mRNA  | Down   | 0      |
| LOC100134228          | mRNA  | Up     | 0      |
| LOC23117              | mRNA  | Down   | 0      |
| LOC338799             | mRNA  | Down   | 0      |
| LOC389831             | mRNA  | Down   | 0      |
| LOC391132             | mRNA  | Up     | 0      |
| LOC391532             | mRNA  | Up     | 0      |
| LOC402360             | mRNA  | Down   | 0      |
| LOC51233              | mRNA  | Up     | 0      |
| LOC595101             | mRNA  | Up     | 0      |
| LOC646909             | mRNA  | Up     | 0      |
| LOC646949             | mRNA  | Up     | 0      |
| LOC649294             | mRNA  | Up     | 0      |
| LOC650392             | mRNA  | Up     | 0      |
| LOC728763             | mRNA  | Down   | 0      |
| LOC728820             | mRNA  | Up     | 0      |
| LOC729046             | mRNA  | Up     | 0      |
| LOC729259             | mRNA  | Up     | 0      |
| LOC729652             | mRNA  | Up     | 0      |
| LOC780529             | mRNA  | Up     | 0      |
| LRIG1                 | mRNA  | Down   | 9      |
| LRP5L                 | mRNA  | Up     | 0      |
| LRRC2                 | mRNA  | Down   | 0      |
| LRRRC36               | mRNA  | Down   | 0      |
| LRRRC45               | mRNA  | Down   | 0      |
| LRRRC46               | mRNA  | Down   | 0      |
| LRRRC75A-AS1          | lncRNA | Plane  | 2      |
| LTB2P2                | mRNA  | Down   | 0      |
| LTB4                  | mRNA  | Down   | 0      |
| LTC45                 | mRNA  | Down   | 0      |
Table 2 (Continued).

| Gene        | RNA   | Up/Down | Degree |
|-------------|-------|---------|--------|
| LTK         | mRNA  | Down    | 0      |
| MACCI-AS1   | IncRNA| Plane   | 1      |
| MAGOH       | mRNA  | Up      | 0      |
| MALAT1      | IncRNA| Plane   | 10     |
| MAOB        | mRNA  | Down    | 0      |
| MAP4K3      | mRNA  | Down    | 11     |
| MAPKAPK3    | mRNA  | Up      | 0      |
| MATN1-AS1   | IncRNA| Plane   | 1      |
| MBD4        | mRNA  | Up      | 0      |
| MBNL1-AS1   | IncRNA| Plane   | 1      |
| MCF2L-AS1   | IncRNA| Plane   | 1      |
| MCM3AP-AS1  | IncRNA| Plane   | 1      |
| MED18       | mRNA  | Up      | 2      |
| MELF-AS1    | IncRNA| Plane   | 1      |
| METTL7A     | mRNA  | Up      | 3      |
| MFAP4       | mRNA  | Down    | 2      |
| MGC70870    | mRNA  | Up      | 0      |
| MIR124-2HG  | IncRNA| Plane   | 1      |
| MIR155HG    | IncRNA| Plane   | 1      |
| MIR17HG     | IncRNA| Plane   | 1      |
| MIR22HG     | IncRNA| Plane   | 2      |
| MIR4435-2HG | IncRNA| Plane   | 2      |
| MIR4458HG   | IncRNA| Plane   | 1      |
| MIR583HG    | IncRNA| Plane   | 1      |
| MIRLET7BH    | IncRNA| Plane   | 4      |
| MKNK1-AS1   | IncRNA| Plane   | 1      |
| MMP1        | mRNA  | Up      | 1      |
| MMP10       | mRNA  | Up      | 0      |
| MMP14       | mRNA  | Down    | 12     |
| MMP19       | mRNA  | Up      | 0      |
| MMP9        | mRNA  | Up      | 49     |
| MNT         | mRNA  | Down    | 0      |
| MOP-1       | mRNA  | Up      | 0      |
| MRTO4       | mRNA  | Up      | 0      |
| M5A2        | mRNA  | Down    | 0      |
| M5A8B       | mRNA  | Down    | 0      |
| MSC         | mRNA  | Up      | 7      |
| MST1        | mRNA  | Down    | 13     |
| MSTOP9      | mRNA  | Down    | 0      |
| MT1F        | mRNA  | Up      | 0      |
| MT1H        | mRNA  | Up      | 0      |
| MT1L        | mRNA  | Up      | 0      |
| MT1M        | mRNA  | Up      | 7      |
| MTNDI-P23   | mRNA  | Up      | 0      |
| MXD1        | mRNA  | Up      | 13     |
| MYB         | mRNA  | Down    | 59     |
| MYH1I       | mRNA  | Down    | 0      |
| MYH2        | mRNA  | Down    | 1      |
| MYO15B      | mRNA  | Down    | 0      |
| MYOC        | mRNA  | Down    | 1      |

(Continued)
Table 2 (Continued).

| Gene          | RNA  | Up/Down | Degree |
|---------------|------|---------|--------|
| MYOZ1         | mRNA | Down    | 0      |
| MYRIP         | mRNA | Down    | 0      |
| NBPF14        | mRNA | Down    | 0      |
| NBPF20        | mRNA | Up      | 0      |
| NCR2          | mRNA | Up      | 0      |
| NEAT1         | lncRNA | Plane | 7      |
| NEUROG1       | mRNA | Up      | 0      |
| NFKBIZ        | mRNA | Up      | 0      |
| NFYC-AS1      | lncRNA | Plane | 2      |
| NKILA         | lncRNA | Plane | 1      |
| NKX2-8        | mRNA | Down    | 0      |
| NLRP2         | mRNA | Up      | 0      |
| NMNAT3        | mRNA | Down    | 0      |
| NNT-AS1       | lncRNA | Plane | 1      |
| NORAD         | lncRNA | Plane | 11     |
| NOV           | mRNA | Down    | 0      |
| NPHP4         | mRNA | Up      | 0      |
| NPIP          | mRNA | Down    | 0      |
| NPM3          | mRNA | Up      | 0      |
| NPNT          | mRNA | Down    | 15     |
| NPPA-AS1      | lncRNA | Plane | 1      |
| NPTN          | mRNA | Down    | 0      |
| NR2F1-AS1     | lncRNA | Plane | 7      |
| NR2F2         | mRNA | Down    | 5      |
| NR4A1         | mRNA | Up      | 0      |
| NR4A2         | mRNA | Up      | 18     |
| NSBP1         | mRNA | Down    | 0      |
| NTF3          | mRNA | Down    | 8      |
| NTM           | mRNA | Up      | 1      |
| NUAK2         | mRNA | Up      | 0      |
| NUTM2A-AS1    | lncRNA | Plane | 1      |
| NUTM2B-AS1    | lncRNA | Plane | 2      |
| OGN           | mRNA | Down    | 0      |
| OIP5-AS1      | lncRNA | Plane | 5      |
| OLFML3        | mRNA | Down    | 0      |
| OLIG3         | mRNA | Up      | 0      |
| OMD           | mRNA | Down    | 0      |
| OPN1LW        | mRNA | Up      | 0      |
| OR2A1-AS1     | lncRNA | Plane | 2      |
| OSM           | mRNA | Up      | 0      |
| OSTbeta       | mRNA | Down    | 0      |
| PABPC4L       | mRNA | Down    | 0      |
| PADI3         | mRNA | Up      | 0      |
| PAX8-AS1      | lncRNA | Plane | 1      |
| PCA3          | lncRNA | Plane | 1      |
| PCBP1-AS1     | lncRNA | Plane | 5      |
| PCDH18        | mRNA | Down    | 0      |
| PCNP          | mRNA | Down    | 0      |
| PCOLCE2       | mRNA | Down    | 0      |
| PDAP1         | mRNA | Up      | 0      |

(Continued)
Table 2 (Continued).

| Gene         | RNA      | Up/Down | Degree |
|--------------|----------|---------|--------|
| PDCD4-AS1    | IncRNA   | Plane   | 1      |
| PF4          | mRNA     | Up      | 0      |
| PFDN6        | mRNA     | Up      | 0      |
| PHF1         | mRNA     | Down    | 0      |
| PHF5A        | mRNA     | Up      | 0      |
| PHLDA1       | mRNA     | Up      | 0      |
| PHLDA2       | mRNA     | Up      | 0      |
| PHLDA3       | mRNA     | Down    | 0      |
| PI6          | mRNA     | Down    | 0      |
| PI3          | mRNA     | Up      | 0      |
| PIK3CD-AS1   | IncRNA   | Plane   | 1      |
| PIK3CD-AS2   | IncRNA   | Plane   | 1      |
| PIM1         | mRNA     | Up      | 19     |
| PINK1-AS     | IncRNA   | Plane   | 11     |
| PLA2G1B      | mRNA     | Down    | 0      |
| PLA2G2A      | mRNA     | Up      | 0      |
| PLA2G7       | mRNA     | Up      | 0      |
| PLEKHG4      | mRNA     | Up      | 0      |
| PLEKHH3      | mRNA     | Down    | 0      |
| PLN          | mRNA     | Down    | 0      |
| PMAIP1       | mRNA     | Up      | 5      |
| POLR2C       | mRNA     | Up      | 0      |
| POLR2J4      | IncRNA   | Plane   | 1      |
| POU2AF1      | mRNA     | Up      | 0      |
| PPIB         | mRNA     | Up      | 0      |
| PPP1R14A     | mRNA     | Down    | 0      |
| PPP1R3C      | mRNA     | Down    | 0      |
| PPP3CB-AS1   | IncRNA   | Plane   | 5      |
| PRDM6        | mRNA     | Down    | 0      |
| PRKCB        | mRNA     | Up      | 3      |
| PRKY         | mRNA     | Down    | 0      |
| PROS1        | mRNA     | Down    | 1      |
| PROSER2-AS1  | IncRNA   | Plane   | 1      |
| PRPF19       | mRNA     | Up      | 0      |
| PRR13P5      | mRNA     | Up      | 0      |
| PRRG4        | mRNA     | Up      | 0      |
| PRRT2        | mRNA     | Down    | 0      |
| PRSS36       | mRNA     | Up      | 0      |
| PSMA3-AS1    | IncRNA   | Plane   | 7      |
| PTCHD1-AS    | IncRNA   | Plane   | 1      |
| PTOV1-AS1    | IncRNA   | Plane   | 1      |
| PTPN1        | mRNA     | Up      | 2      |
| PTPRD        | mRNA     | Down    | 12     |
| PTX3         | mRNA     | Up      | 3      |
| PVAT1        | IncRNA   | Plane   | 2      |
| QTRT1        | mRNA     | Up      | 0      |
| RAB13        | mRNA     | Up      | 3      |
| RAB20        | mRNA     | Up      | 0      |
| RAB23        | mRNA     | Down    | 4      |
| RAET1E-AS1   | IncRNA   | Plane   | 1      |

(Continued)
Table 2 (Continued).

| Gene         | RNA    | Up/down | Degree |
|--------------|--------|---------|--------|
| RANBP6       | mRNA   | Down    | 0      |
| RAP1GAP      | mRNA   | Down    | 0      |
| RAPGEF5      | mRNA   | Down    | 0      |
| RBM26-AS1    | lncRNA | Plane   | 1      |
| RERG         | mRNA   | Down    | 0      |
| RFX3-AS1     | lncRNA | Plane   | 4      |
| RGL2         | mRNA   | Down    | 0      |
| RGL4         | mRNA   | Up      | 0      |
| RGS1         | mRNA   | Up      | 0      |
| RGS22        | mRNA   | Down    | 0      |
| RND1         | mRNA   | Up      | 0      |
| RNF125       | mRNA   | Up      | 0      |
| RNF145       | mRNA   | Up      | 0      |
| RPI-117O3.2  | lncRNA | Plane   | 1      |
| RPI-118J21.5 | lncRNA | Plane   | 6      |
| RPI-158P9.1  | lncRNA | Plane   | 1      |
| RPI-191J18.66| lncRNA | Plane   | 10     |
| RPI-193H18.2 | lncRNA | Plane   | 1      |
| RPI-199J3.7  | lncRNA | Plane   | 4      |
| RPI-224A6.9  | lncRNA | Plane   | 1      |
| RPI-253P7.4  | lncRNA | Plane   | 1      |
| RPI-27K12.2  | lncRNA | Plane   | 1      |
| RPI-283E3.8  | lncRNA | Plane   | 2      |
| RPI-37C10.3  | lncRNA | Plane   | 2      |
| RPI-92O14.6  | lncRNA | Plane   | 3      |
| RPI1-1000B6.5| lncRNA | Plane   | 1      |
| RPI1-1007O24.3| lncRNA | Plane   | 4      |
| RPI1-106M3.3  | lncRNA | Plane   | 1      |
| RPI1-108M9.3  | lncRNA | Plane   | 2      |
| RPI1-108M9.6  | lncRNA | Plane   | 2      |
| RPI1-10K16.1  | lncRNA | Plane   | 1      |
| RPI1-1149O23.2| lncRNA | Plane   | 1      |
| RPI1-120D5.1  | lncRNA | Plane   | 2      |
| RPI1-120E11.2 | lncRNA | Plane   | 1      |
| RPI1-133K1.11 | lncRNA | Plane   | 1      |
| RPI1-140H17.2 | lncRNA | Plane   | 1      |
| RPI1-147L13.12 | lncRNA | Plane   | 2      |
| RPI1-154D6.1  | lncRNA | Plane   | 1      |
| RPI1-156E6.1  | lncRNA | Plane   | 3      |
| RPI1-157P1.4  | lncRNA | Plane   | 3      |
| RPI1-158K1.3  | lncRNA | Plane   | 1      |
| RPI1-160H22.5 | lncRNA | Plane   | 1      |
| RPI1-161H23.9 | lncRNA | Plane   | 1      |
| RPI1-161M6.2  | lncRNA | Plane   | 3      |
| RPI1-16E12.2  | lncRNA | Plane   | 1      |
| RPI1-186B7.4  | lncRNA | Plane   | 1      |
| RPI1-197N18.2 | lncRNA | Plane   | 1      |
| RPI1-197N18.8 | lncRNA | Plane   | 1      |
| RPI1-228B15.4 | lncRNA | Plane   | 2      |
| RPI1-244H3.1  | lncRNA | Plane   | 1      |

(Continued)
| Gene      | RNA   | Upordown | Degree |
|-----------|-------|----------|--------|
| RP11-267M23.1 | IncRNA | Plane | 1      |
| RP11-277P12.20 | IncRNA | Plane | 1      |
| RP11-278C7.3 | IncRNA | Plane | 3      |
| RP11-288L9.4 | IncRNA | Plane | 3      |
| RP11-295P9.3 | IncRNA | Plane | 1      |
| RP11-299J3.8 | IncRNA | Plane | 3      |
| RP11-29G8.3 | IncRNA | Plane | 3      |
| RP11-2C24.3  | IncRNA | Plane | 1      |
| RP11-2C24.4  | IncRNA | Plane | 2      |
| RP11-303E16.2| IncRNA | Plane | 2      |
| RP11-304L19.13| IncRNA | Plane | 1      |
| RP11-305E6.4 | IncRNA | Plane | 7      |
| RP11-314B1.2 | IncRNA | Plane | 7      |
| RP11-317N8.5 | IncRNA | Plane | 8      |
| RP11-328C8.4 | IncRNA | Plane | 7      |
| RP11-334C17.5| IncRNA | Plane | 4      |
| RP11-342K2.1 | IncRNA | Plane | 2      |
| RP11-342M1.3 | IncRNA | Plane | 2      |
| RP11-345P4.4 | mRNA  | Down   | 0      |
| RP11-349N5.7 | IncRNA | Plane | 1      |
| RP11-348P0.2 | IncRNA | Plane | 1      |
| RP11-352G18.2| IncRNA | Plane | 3      |
| RP11-355B11.2| IncRNA | Plane | 1      |
| RP11-357H14.17| IncRNA | Plane | 5      |
| RP11-359B12.2| IncRNA | Plane | 1      |
| RP11-360N9.2 | IncRNA | Plane | 1      |
| RP11-372K14.2| IncRNA | Plane | 4      |
| RP11-373N22.3| IncRNA | Plane | 1      |
| RP11-378J18.8| IncRNA | Plane | 1      |
| RP11-380L11.4| IncRNA | Plane | 1      |
| RP11-381N20.1| IncRNA | Plane | 3      |
| RP11-386G11.5| IncRNA | Plane | 5      |
| RP11-394O2.3 | IncRNA | Plane | 1      |
| RP11-395G23.3| IncRNA | Plane | 3      |
| RP11-399K21.14| IncRNA | Plane | 2      |
| RP11-405O10.2| IncRNA | Plane | 1      |
| RP11-412P11.1| IncRNA | Plane | 1      |
| RP11-415J8.3 | IncRNA | Plane | 5      |
| RP11-416N4.4 | IncRNA | Plane | 2      |
| RP11-421L21.3| IncRNA | Plane | 6      |
| RP11-446H18.5| IncRNA | Plane | 1      |
| RP11-452F19.3| IncRNA | Plane | 1      |
| RP11-45P15.4 | IncRNA | Plane | 3      |
| RP11-468E2.5 | IncRNA | Plane | 7      |
| RP11-46O21.2 | IncRNA | Plane | 1      |
| RP11-477D19.2| IncRNA | Plane | 1      |
| RP11-478C19.2| IncRNA | Plane | 2      |
| RP11-481C4.2 | IncRNA | Plane | 1      |
| RP11-493P1.2 | IncRNA | Plane | 3      |
| RP11-519G16.3| IncRNA | Plane | 1      |

(Continued)
| Gene                     | RNA    | Updown | Degree |
|--------------------------|--------|--------|--------|
| RP11-531A24.7            | lncRNA | Plane  | 1      |
| RP11-539I5.1             | lncRNA | Plane  | 2      |
| RP11-545I5.3             | lncRNA | Plane  | 4      |
| RP11-54O7.1              | lncRNA | Plane  | 1      |
| RP11-54O7.3              | lncRNA | Plane  | 10     |
| RP11-574K11.29           | lncRNA | Plane  | 1      |
| RP11-57H12.5             | lncRNA | Plane  | 5      |
| RP11-588H23.3            | lncRNA | Plane  | 1      |
| RP11-588K22.2            | lncRNA | Plane  | 4      |
| RP11-58K22.5             | lncRNA | Plane  | 1      |
| RP11-5C23.1              | lncRNA | Plane  | 1      |
| RP11-60A24.3             | lncRNA | Plane  | 1      |
| RP11-626G11.5            | lncRNA | Plane  | 1      |
| RP11-631M21.2            | mRNA   | Down   | 0      |
| RP11-656D10.6            | lncRNA | Plane  | 1      |
| RP11-656D10.7            | lncRNA | Plane  | 2      |
| RP11-65L3.2              | lncRNA | Plane  | 2      |
| RP11-661A12.5            | lncRNA | Plane  | 1      |
| RP11-661A12.8            | lncRNA | Plane  | 1      |
| RP11-677I18.3            | lncRNA | Plane  | 1      |
| RP11-677M14.8            | lncRNA | Plane  | 3      |
| RP11-69E11.4             | lncRNA | Plane  | 11     |
| RP11-69E11.8             | lncRNA | Plane  | 3      |
| RP11-701H24.4            | lncRNA | Plane  | 1      |
| RP11-702F3.1             | lncRNA | Plane  | 1      |
| RP11-714G18.1            | lncRNA | Plane  | 1      |
| RP11-715F3.2             | lncRNA | Plane  | 3      |
| RP11-73M18.8             | lncRNA | Plane  | 1      |
| RP11-77H9.2              | lncRNA | Plane  | 1      |
| RP11-793H13.3            | lncRNA | Plane  | 2      |
| RP11-799B12.4            | lncRNA | Plane  | 1      |
| RP11-802E16.3            | lncRNA | Plane  | 1      |
| RP11-815J21.4            | lncRNA | Plane  | 1      |
| RP11-819C21.1            | lncRNA | Plane  | 2      |
| RP11-81K13.1             | lncRNA | Plane  | 2      |
| RP11-822E23.8            | lncRNA | Plane  | 5      |
| RP11-829H16.3            | lncRNA | Plane  | 1      |
| RP11-834C11.4            | lncRNA | Plane  | 6      |
| RP11-843B15.4            | lncRNA | Plane  | 3      |
| RP11-84G21.1             | lncRNA | Plane  | 1      |
| RP11-861E21.2            | lncRNA | Plane  | 1      |
| RP11-96A15.8             | lncRNA | Plane  | 1      |
| RP11-96D1.10             | lncRNA | Plane  | 2      |
| RP11-983P16.4            | lncRNA | Plane  | 1      |
| RP13-143G15.4            | lncRNA | Plane  | 1      |
| RP13-36C9.6              | mRNA   | Down   | 0      |
| RP13-39P12.3             | lncRNA | Plane  | 1      |
| RP13-516M14.1            | lncRNA | Plane  | 1      |
| RP3-323N1.2              | lncRNA | Plane  | 1      |
| RP3-467L1.4              | lncRNA | Plane  | 2      |
Table 2 (Continued).

| Gene          | RNA     | Up/down | Degree |
|---------------|---------|---------|--------|
| RP4-569M23.2  | lncRNA  | Plane   | 1      |
| RP4-605G3.4   | lncRNA  | Plane   | 1      |
| RP4-613B23.1  | lncRNA  | Plane   | 1      |
| RP4-622L5.7   | lncRNA  | Plane   | 1      |
| RP4-625H18.2  | lncRNA  | Plane   | 1      |
| RP4-635E18.7  | lncRNA  | Plane   | 2      |
| RP4-639F20.1  | lncRNA  | Plane   | 1      |
| RP4-665N4.8   | lncRNA  | Plane   | 2      |
| RP4-669K10.8  | lncRNA  | Plane   | 3      |
| RP4-671G15.2  | lncRNA  | Plane   | 2      |
| RP4-671O14.6  | lncRNA  | Plane   | 3      |
| RP4-758J18.13 | lncRNA  | Plane   | 1      |
| RP4-758J18.2  | lncRNA  | Plane   | 1      |
| RP5-761J14.8  | lncRNA  | Plane   | 1      |
| RP5-794H19.1  | lncRNA  | Plane   | 1      |
| RP5-1021J20.5 | lncRNA  | Plane   | 1      |
| RP5-1024G6.2  | lncRNA  | Plane   | 2      |
| RP5-1024G6.5  | lncRNA  | Plane   | 6      |
| RP5-1033H22.2 | lncRNA  | Plane   | 1      |
| RP5-1039K5.19 | lncRNA  | Plane   | 3      |
| RP5-1071N3.1  | lncRNA  | Plane   | 1      |
| RP5-1074L1.4  | lncRNA  | Plane   | 3      |
| RP5-1101C3.1  | lncRNA  | Plane   | 1      |
| RP5-1126H10.2 | lncRNA  | Plane   | 3      |
| RP5-1198O20.4 | lncRNA  | Plane   | 8      |
| RP5-864K19.7  | lncRNA  | Plane   | 7      |
| RP5-884C9.2   | lncRNA  | Plane   | 1      |
| RP5-894A10.6  | lncRNA  | Plane   | 1      |
| RP5-899E9.1   | lncRNA  | Plane   | 4      |
| RP5-991G20.1  | lncRNA  | Plane   | 1      |
| RP5-997D16.2  | lncRNA  | Plane   | 1      |
| RP6-24A23.7   | lncRNA  | Plane   | 1      |
| RPA4          | mRNA    | Down    | 0      |
| RPS14P8       | mRNA    | Up      | 0      |
| RPS6P1        | mRNA    | Down    | 0      |
| RRP12         | mRNA    | Up      | 0      |
| RSPH10B       | mRNA    | Down    | 0      |
| S100A12       | mRNA    | Up      | 0      |
| S100A8        | mRNA    | Up      | 0      |
| S100A9        | mRNA    | Up      | 1      |
| S100B         | mRNA    | Up      | 3      |
| SAA1          | mRNA    | Up      | 0      |
| SAPS1         | mRNA    | Down    | 0      |
| SCAMP1-AS1    | lncRNA  | Plane   | 1      |
| SCN4B         | mRNA    | Down    | 0      |
| SEC14L3       | mRNA    | Down    | 0      |
| 14-Sep        | mRNA    | Up      | 0      |
| SERPIND1      | mRNA    | Up      | 0      |
| SERTAD1       | mRNA    | Up      | 0      |
| SETBP1        | mRNA    | Down    | 0      |
Table 2 (Continued).

| Gene       | RNA    | Up/Down | Degree |
|------------|--------|---------|--------|
| SFN        | mRNA   | Up      | 0      |
| SFTPA1B    | mRNA   | Down    | 0      |
| SGCE       | mRNA   | Down    | 0      |
| SGMS1-AS1  | lncRNA | Plane   | 1      |
| SGPP2      | mRNA   | Up      | 5      |
| SH3BP5-AS1 | lncRNA | Plane   | 1      |
| SH3GL3     | mRNA   | Down    | 0      |
| SHANK3     | mRNA   | Down    | 0      |
| SHC2       | mRNA   | Down    | 0      |
| SLAMF7     | mRNA   | Up      | 0      |
| SLC16A1-AS1| lncRNA | Plane   | 1      |
| SLC25A22   | mRNA   | Up      | 0      |
| SLC26A4    | mRNA   | Up      | 0      |
| SLC2A1-AS1 | lncRNA | Plane   | 3      |
| SLC39A7    | mRNA   | Up      | 0      |
| SLC44A1    | mRNA   | Down    | 0      |
| SLC45A4    | mRNA   | Down    | 0      |
| SLC6A19    | mRNA   | Up      | 0      |
| SLC6A4     | mRNA   | Down    | 10     |
| SLC7A8     | mRNA   | Up      | 0      |
| SLC04A1    | mRNA   | Up      | 0      |
| SLFN1-AS1  | lncRNA | Plane   | 17     |
| SLIT12     | mRNA   | Down    | 0      |
| SLITRK6    | mRNA   | Down    | 0      |
| SMAD7      | mRNA   | Down    | 75     |
| SMARCA3    | mRNA   | Down    | 0      |
| SMG7       | mRNA   | Down    | 0      |
| SNAI1      | mRNA   | Up      | 41     |
| SNHG1      | lncRNA | Plane   | 2      |
| SNHG12     | lncRNA | Plane   | 22     |
| SNHG14     | lncRNA | Plane   | 1      |
| SNHG15     | lncRNA | Plane   | 2      |
| SNHG16     | lncRNA | Plane   | 6      |
| SNHG17     | lncRNA | Plane   | 1      |
| SNHG20     | lncRNA | Plane   | 1      |
| SNHG22     | lncRNA | Plane   | 2      |
| SNHG3      | lncRNA | Plane   | 3      |
| SNHG5      | lncRNA | Plane   | 3      |
| SNHG7      | lncRNA | Plane   | 5      |
| SNORA70    | mRNA   | Down    | 0      |
| SNTN       | mRNA   | Down    | 0      |
| SOCS3      | mRNA   | Up      | 15     |
| SOD2       | mRNA   | Up      | 7      |
| SOSTDC1    | mRNA   | Down    | 0      |
| SPAG8      | mRNA   | Down    | 0      |
| SPARCL1    | mRNA   | Down    | 0      |
| SPEG       | mRNA   | Down    | 0      |
| SPPI       | mRNA   | Up      | 10     |
| SPSB2      | mRNA   | Down    | 0      |
| SRD5A3-AS1 | lncRNA | Plane   | 1      |

(Continued)
**Table 2 (Continued).**

| Gene           | RNA   | Up/Down | Degree |
|----------------|-------|---------|--------|
| SRGN           | mRNA  | Up      | 0      |
| SSBP3-AS1      | IncRNA| Plane   | 4      |
| SSPN           | mRNA  | Down    | 0      |
| ST20-AS1       | IncRNA| Plane   | 2      |
| ST6GALNAC3     | mRNA  | Down    | 0      |
| ST6GALNAC5     | mRNA  | Down    | 0      |
| STARD13-AS     | IncRNA| Plane   | 3      |
| STARD4-AS1     | IncRNA| Plane   | 4      |
| STC2           | mRNA  | Up      | 5      |
| STK32C         | mRNA  | Up      | 0      |
| STOML3         | mRNA  | Down    | 0      |
| STX18-AS1      | IncRNA| Plane   | 1      |
| SULT1A1        | mRNA  | Down    | 0      |
| SVIL           | mRNA  | Down    | 0      |
| TAF5L          | mRNA  | Up      | 0      |
| TARID          | IncRNA| Plane   | 1      |
| TBC1D9         | mRNA  | Down    | 1      |
| tcag7.873      | mRNA  | Up      | 0      |
| TCEAL4         | mRNA  | Down    | 0      |
| TCF21          | mRNA  | Down    | 2      |
| TCTN2          | mRNA  | Down    | 0      |
| TDRD10         | mRNA  | Down    | 0      |
| TEPI           | mRNA  | Up      | 0      |
| TEX41          | IncRNA| Plane   | 2      |
| THBS1          | mRNA  | Up      | 14     |
| THCAT158       | IncRNA| Plane   | 1      |
| THUMPD3-AS1    | IncRNA| Plane   | 5      |
| TLX1NB         | IncRNA| Plane   | 1      |
| TM3C-AS1       | IncRNA| Plane   | 1      |
| TMED9          | mRNA  | Up      | 0      |
| TMEM100        | mRNA  | Down    | 2      |
| TMEM120B       | mRNA  | Up      | 0      |
| TMEM147-AS1    | IncRNA| Plane   | 2      |
| TMEM178        | mRNA  | Down    | 0      |
| TMEM20I        | mRNA  | Up      | 0      |
| TMEM212        | mRNA  | Down    | 0      |
| TMEM254-AS1    | IncRNA| Plane   | 1      |
| TNFAIP6        | mRNA  | Up      | 3      |
| TNFRSF1A       | mRNA  | Up      | 0      |
| TNFRSF6B       | mRNA  | Up      | 0      |
| TONSL-AS1      | IncRNA| Plane   | 1      |
| TPTEP1         | mRNA  | Up      | 0      |
| TRAM2-AS1      | IncRNA| Plane   | 1      |
| TREM2          | mRNA  | Up      | 2      |
| TRG-AS1        | IncRNA| Plane   | 7      |
| TSC22D1-AS1    | IncRNA| Plane   | 1      |
| TSIX           | IncRNA| Plane   | 3      |
| TTMA           | mRNA  | Up      | 0      |
| TTN-AS1        | IncRNA| Plane   | 5      |
| TTTY15         | mRNA  | Down    | 0      |

(Continued)
Table 2 (Continued).

| Gene       | RNA     | Up/Down | Degree |
|------------|---------|---------|--------|
| TUBA4B     | mRNA    | Down    | 0      |
| TUFM       | mRNA    | Down    | 0      |
| TUG1       | lncRNA  | Plane   | 6      |
| TXLNGY     | mRNA    | Down    | 0      |
| TYRPI      | mRNA    | Down    | 0      |
| UBD        | mRNA    | Up      | 5      |
| UNK        | mRNA    | Up      | 0      |
| UNQ6494    | lncRNA  | Plane   | 1      |
| UNQ9419    | mRNA    | Up      | 0      |
| UPF1       | mRNA    | Up      | 0      |
| URB2       | mRNA    | Up      | 0      |
| USP36      | mRNA    | Up      | 0      |
| VCAN-AS1   | lncRNA  | Plane   | 3      |
| VLDLR-AS1  | lncRNA  | Plane   | 1      |
| VPS18      | mRNA    | Down    | 1      |
| VP59D1-AS1 | lncRNA  | Plane   | 2      |
| WDR67      | mRNA    | Down    | 0      |
| WFDC1      | mRNA    | Down    | 0      |
| WFDC21P    | lncRNA  | Plane   | 2      |
| XAGE1D     | mRNA    | Up      | 0      |
| XIST       | lncRNA  | Plane   | 16     |
| XX-FW83563B9.5 | lncRNA | Plane | 1   |
| XXbac-B461K10.4 | lncRNA | Plane | 5   |
| YEATS2-AS1 | lncRNA  | Plane   | 1      |
| ZACN       | mRNA    | Down    | 0      |
| ZBBX       | mRNA    | Down    | 0      |
| ZBED2      | mRNA    | Down    | 0      |
| ZBTB20-AS1 | lncRNA  | Plane   | 1      |
| ZC3H12A    | mRNA    | Up      | 2      |
| ZEB1-AS1   | lncRNA  | Plane   | 2      |
| ZFHX2-AS1  | lncRNA  | Plane   | 1      |
| ZFP62      | mRNA    | Down    | 0      |
| ZFPM2-AS1  | lncRNA  | Plane   | 7      |
| ZIM2-AS1   | lncRNA  | Plane   | 1      |
| ZNF117     | mRNA    | Up      | 0      |
| ZNF213-AS1 | lncRNA  | Plane   | 2      |
| ZNF264     | mRNA    | Up      | 0      |
| ZNF280D    | mRNA    | Down    | 0      |
| ZNF337-AS1 | lncRNA  | Plane   | 4      |
| ZNF426     | mRNA    | Up      | 0      |
| ZNF572     | mRNA    | Down    | 0      |
| ZNF652     | mRNA    | Up      | 2      |
| ZNF674-AS1 | lncRNA  | Plane   | 3      |
| ZNF675     | mRNA    | Up      | 0      |
| ZNF728     | mRNA    | Up      | 0      |
| ZNF790-AS1 | lncRNA  | Plane   | 8      |
| ZRANB2-AS2 | lncRNA  | Plane   | 1      |
| ZSCAN10    | mRNA    | Up      | 0      |
High-throughput sequencing technologies have implied in various disease for detecting potential diagnostic and prognostic biomarkers at the transcriptome level. Accumulation of studies revealed the disease-related RNAs which correlated with disease pathology. IncRNAs and miRNAs regulated mRNAs network implied in the various diseases, and some of them was identified as potentially suitable biomarkers. In this study, we identified the differentially expressed RNAs, which have significant associations with immune and cancer-related signaling pathway. Among of these, the cytokine receptor CXCR2 antagonist (MK-7123) reduced the chemotaxis of neutrophils, which may alleviate the airway inflammation of COPD. The p53 signaling pathway polymorphism was associated with changes in emphysema in COPD patients.

In addition, ceRNAs network related to COPD was evaluated, implying new molecular mechanism and potential therapeutic target for COPD. Among of the network genes, 10 IncRNAs might be used as COPD marker including SNHG12, SLFN1L1-AS1, KCNQ1OT1, XIST, EAF1-AS1, FOXD2-AS1, NORAD, PINK1-AS and RP11-69E11.4. Among them, SNHG12 participated in the unfolded protein response and function as a potential therapeutic target and biomarker for human cancer. Many tumor cells avoided immune-mediated attacks and enhanced the polarization of effector immune cells (such as macrophages and T cells) via SNHG12. SNHG12 also acted as a competitive endogenous RNA (ceRNA) by containing multiple miRNA binding sites, thereby “sponging” these miRNAs to regulate its downstream targets. Recent studies have described the emerging role of ceRNAs in the etiology of cancer, where various ncRNA molecules including IncRNAs, miRNAs, pseudogenes and circular RNAs (circRNAs) share common miRNA response elements (MREs), thereby passing through complex RNA networks Mutual regulation through cellular processes. XIST/miR-200c-3p/EGR3 axis promotes 16HBE cell apoptosis and inflammatory response stimulated by cigarette smoke extract. These findings may provide new insights for the treatment of COPD by reducing lung inflammation.

In conclusion, our research has revealed the DEGs and DEmis related to COPD, and constructed the ceRNA network in COPD, which may provide potential new insights for the treatment of COPD. However, we have some limitations on the mechanism of action of IncRNA involved in the progression of chronic obstructive pulmonary disease. Next, we will further study the related functions and mechanisms through cell, tissue and animal experiments.

**Abbreviations**

COPD, Chronic obstructive pulmonary disease; GEO, Gene Expression Omnibus; DEGs, differentially expressed genes; DEmi, differentially expressed miRNAs; IncRNA, Long non-coding RNA; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes.
Data Sharing Statement
The datasets generated during and/or analyzed during the current study are available in the Gene Expression Omnibus (GEO) datasets (http://www.ncbi.nlm.nih.gov/geo/).

Ethical Approval
This study has been exempted from the medical ethics committee of the Affiliated Hospital of Inner Mongolia Medical University. The public database mentioned in this study is publicly available for re-analyzing, and no ethical approval was required by the local ethics committees, so that this study does not require ethics approval.

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Disclosure
The authors declare that they have no competing interests in this work.

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