Long non-coding RNAs RP5-821D11.7, APCDD1L-AS1 and RP11-277P12.9 were associated with the prognosis of lung squamous cell carcinoma

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Abstract. Lung squamous cell carcinoma (LUSC), a type of non-small cell lung carcinoma, has a poor therapeutic response, high relapse rate and poor prognosis. The present study was designed to reveal the key long non-coding RNAs (lncRNAs) associated with the prognosis of LUSC. The lncRNA expression profiles of LUSC and adjacent samples were downloaded from The Cancer Genome Atlas database. Based on the edgeR and DEseq packages, the differentially expressed lncRNAs (DElNs) between LUSC and adjacent samples were obtained and the intersecting DElNs were regarded as significant DElNs. Subsequently, a prognostic risk model was established using Cox regression analysis and its classification effect was detected by survival analysis. Using survival analysis, the effect of the prognostic risk model was assessed in the validation set by survival analysis. Using survival analysis, the effect of the prognostic risk model was assessed in the validation set.

Introduction

Lung cancer, including small cell lung carcinoma and non-small cell lung carcinoma (NSCLC), is the primary cause of cancer death globally (1). NSCLC consists of lung squamous cell carcinoma (LUSC), adenocarcinoma and large cell carcinoma (2), which are responsible for 80% of lung cancer mortality (3). LUSC is associated with tobacco smoking, and more frequently occurs in men (4). It has the characteristics of poor therapeutic response, high relapse rate and poor prognosis (5), inducing ~400,000 mortalities/year worldwide (6). Therefore, revealing the genes involved in the prognosis of LUSC is of great importance.

Long non-coding RNAs (lncRNAs) are a class of non-protein-coding RNAs that mediate gene expression, which play important roles in multiple biological processes and diverse carcinomas (7). Previous studies have identified a number of lncRNAs to be associated with prognosis of LUSC. For example, Zhang et al. (8) reported that lncRNA 1133 (LINC01133) is overexpressed in patients with LUSC and may shorten their survival time, thus LINC01133 is a promising biomarker for LUSC. The lncRNA metastasis associated lung adenocarcinoma transcript 1 is reported to have tumor-promoting functions and is associated with the survival time of patients with NSCLC (9,10). The lncRNA HOX transcript antisense intergenic RNA (HOTAIR) mediates the cell invasion and metastasis of NSCLC by downregulating homeobox A5, indicating that HOTAIR may serve as a prognostic marker and therapeutic target in patients with NSCLC (11,12). By inhibiting the expression of Kruppel like factor 2 (KLF2) and p21, lncRNA antisense non-coding RNA in the INK4 locus promotes cell proliferation and suppresses...
cellular apoptosis NSCLC (13,14). Furthermore, IncRNA associated with microvascular invasion in HCC regulates NSCLC cell proliferation and invasion, thus its overexpression may be used as a prognostic biomarker for NSCLC (15). However, the IncRNAs associated with the prognosis of LUSC have not been completely elucidated.

The present study further examined the key IncRNAs associated with the prognosis of LUSC through a series of bioinformatics methods. The IncRNA expression profiles of LUSC were downloaded from The Cancer Genome Atlas, and the differentially expressed IncRNAs (DELs) between LUSC and adjacent samples were identified. Following prognosis-associated DEL screening, a prognostic risk model was established and evaluated. Finally, the co-expression genes of important IncRNAs were obtained and their functions were predicted. The present study may contribute to predicting the prognosis of LUSC and revealing novel molecules associated with the disease.

Materials and methods

Data source. The IncRNA expression profiles of LUSC and the relevant clinical data were downloaded from The Cancer Genome Atlas (TCGA; cancergenome.nih.gov) database (downloaded on April 18, 2017). Samples without clinical data were removed and the data of 501 patients were obtained (Table I). In addition, the data of 49 tumor-adjacent normal lung tissues were obtained.

DEL screening. Subsequent to obtaining the RNA-sequencing data of LUSC from TCGA, IncRNA annotation was performed using the GENCODE database (www.gencodegenes.org) (16). The IncRNAs with average expression values (counts/million) >0.1 were considered as sample expressing IncRNAs. The two independent R (version 3.1.0) (17) packages edgeR (version 3.8.5; www.bioconductor.org/packages/release/bioc/html/edgeR.html) (18) and DESeq (version 1.16.0; www.bioconductor.org/packages/release/bioc/html/DESeq.html) (19) were used for screening DELs between LUSC samples and adjacent samples. The adjusted P-value <0.05 and llog fold change (FC) >1 were set as thresholds. The intersecting DELs predicted by the edgeR and DESeq packages were regarded as significant DELs.

Establishment of prognostic risk model. The DELs expressed in <10% of LUSC samples and patients with a survival time of <30 days were eliminated. The patients were randomly divided into a test set and validation set. For the test set, Cox univariate regression analysis was used to analyze the correlation between DELs and overall survival (OS). The IncRNAs with a P-value <0.05 was screened as prognosis-associated DELs. Subsequently, these prognosis-associated DELs were analyzed using Cox multivariate regression analysis to establish the prognostic risk model, with P-value <0.05 as the threshold. The prognosis risk score was calculated using the following formula (20):

Prognosis risk score = expression value of gene 1 x risk coefficient of gene 1 + expression value of gene 2 x risk coefficient of gene 2 + expression value of gene 3 x risk coefficient of gene 3.

In the test set, the expression levels of the prognosis-associated DELs in cancerous samples and adjacent samples were compared using the non-parametric Wilcoxon signed-rank test.

Detection of the classification effect of the prognostic risk model. The test set was divided into a high risk group and a low risk group, according to the median prognostic risk score. To assess the effect of prognostic risk score in determining the prognosis of patients, the difference between the survival curves of the high and low risk groups was analyzed by drawing receiver operating characteristic (ROC) curves using survivalROC package (version 1.0.3; https://cran.r-project.org/web/packages/survivalROC/index.html).

Determination of the correlation between prognostic risk score and prognosis. Using Cox univariate regression analysis, the correlation between prognostic risk score and clinical characteristics, including the OS of patients, were further analyzed. Subsequently, Cox multivariate regression analysis was applied to determine whether the prognostic risk score was an independent prognostic factor. A P-value <0.05 was set as the threshold value. The hazard ratio and its 95% confidence intervals were used for evaluation. In order to avoid the assessment of the survival curve with a different pattern or shape, a log rank test was used. Based on a χ² test (23), the correlations between DELs and clinical characteristics were detected. In addition, ROC curves were used to assess the prediction significance of the prognostic risk score following treatment, with the two-sided P-value <0.05 as the threshold.

Functional analysis of important IncRNAs. Associated genes (co-expression genes) of IncRNAs were obtained through the Human RNAsq expression data platform in the Multi-Experiment Matrix (MEM; biit.cs.ut.ee/mem/index.cgi) online tool (24). Using the STRING database (string-db.org) (25), a protein-protein interaction (PPI) network was established, with an associated score >0.4 and a number of associated nodes >3 set as the thresholds. Subsequently, the PPI network of IncRNAs and their associated genes was visualized using Cytoscape software 3.5.1 (www.cytoscape.org) (26). Additionally, Gene Ontology (GO; www.geneontology.org) (27) and Kyoto Encyclopedia of Genes and Genomes (KEGG; www.genome.ad.jp/kegg) (28) pathway enrichment analyses were performed based on the Database for Annotation, Visualization and Integrated Discovery (DAVID 6.7; david.ncifcrf.gov) (29) bioinformatics tool, with a P-value <0.05 set as the threshold.

Results

DEL screening. A total of 5,515 DELs were identified between LUSC samples and adjacent samples, including 2,537 DELs from the edgeR package and 2,048 DELs from the DESeq
package. Finally, a total of 2,041 significant DELs were obtained by selecting the intersecting DELs predicted by the edgeR and DEseq packages. The heatmap of the 2,041 DELs is presented in Fig. 1, indicating that the lncRNA expression profiles of LUSC and adjacent samples were different.

Establishment of the prognostic risk model. A total of 489 samples and 1,468 DELs were included in the survival analysis. The patients were randomly divided into test (n=245) and validation (n=244) sets. Cox univariate regression analysis demonstrated that there were 68 prognosis-associated DELs in the test set. Subsequently, Cox multivariate regression analysis indicated that 3 prognosis-associated DELs (including RP5-821D11.7, APCDD1L-AS1 and RP11-277P12.9) had important prognostic value. The prognostic risk score was calculated using the following formula: Prognostic risk score = expression value of RP5-821D11.7 x (-0.392) + expression value of APCDD1L-AS1 x (0.101) + expression value of RP11-277P12.9 x (-0.114).

In the test set, the expression levels of the three prognosis-associated DELs in LUSC samples and adjacent samples were compared by non-parametric Wilcoxon signed-rank test. As presented in Fig. 2, the expression levels were significantly increased in LUSC samples compared with adjacent samples (P<0.05; Fig. 2). In addition, the expression levels of the three prognosis-associated DELs were able to be used to separate LUSC samples from the adjacent samples with an area under the ROC curve (AUC) >0.8 (Fig. 3A-C). Furthermore, the KM survival analysis demonstrated that the samples with high expression levels of the three prognosis-associated DELs had significantly lower OS compared with those with low expression levels (P<0.05; Fig. 3D-F).

Detection of the classification effect of the prognostic risk model. The KM survival analysis indicated that the samples in the high risk group (OS, 769.1±713.3 days) had a significantly lower OS compared with those in the low risk group (OS, 1240.0±1030.1 days) (P=0.00097) (Fig. 4A). The ROC curve demonstrated that the prognostic risk scores were able to predict the 5-year survival of patients to a certain degree (AUC, 0.68; Fig. 4B).

Evaluation of prognostic risk as an independent prognostic factor. Cox univariate regression analysis demonstrated that certain clinical characteristics were associated with the OS of patients, including risk score (P<0.001), neoplasm recurrence (P<0.001), tumor-node-metastasis (TNM) stage (P<0.001), tobacco smoking history (P=0.028), M stage (P=0.030), and T stage (P=0.038) (Table II). However, Cox multivariate regression analysis suggested that only risk score (P<0.001), and tobacco smoking history (P=0.048) had potential as independent prognostic factors (Table III).

In addition, the correlation between prognostic risk scores and other clinical characteristics were evaluated. ROC curves demonstrated that prognostic risk scores were correlated with distant metastasis (pM) (P<0.001; Fig. 5A), tumor recurrence (P=0.038; Fig. 5B) and residual tumor (P=0.001; Fig. 5C). In particular, pM had the highest correlation with prognostic risk scores, indicating that the three prognosis-associated DELs may serve important roles in the distant metastasis of LUSC.

Table I. Clinical characteristics of patients (n=501) with lung squamous cell carcinoma in the present study.

| Variable                        | No. patients |
|---------------------------------|--------------|
| Age, years                      |              |
| ≤65                             | 190          |
| >65                             | 311          |
| Sex                             |              |
| Female                          | 139          |
| Male                            | 362          |
| Pathological stage              |              |
| I                               | 244          |
| II                              | 162          |
| III                             | 84           |
| IV                              | 7            |
| NA                              | 4            |
| T stage                         |              |
| T1                              | 114          |
| T2                              | 293          |
| T3                              | 71           |
| T4                              | 23           |
| N stage                         |              |
| N0                              | 319          |
| N1                              | 131          |
| N2-N3                           | 45           |
| NA                              | 6            |
| M stage                         |              |
| M0                              | 411          |
| M1                              | 7            |
| NA                              | 83           |
| Radiotherapy                    |              |
| Yes                             | 53           |
| No                              | 384          |
| NA                              | 64           |
| Targeted molecular therapy      |              |
| Yes                             | 133          |
| No                              | 306          |
| NA                              | 62           |
| Residual tumor                  |              |
| R0                              | 398          |
| R1+R2                           | 16           |
| NA                              | 87           |
| Neoplasm recurrence             |              |
| Yes                             | 135          |
| No                              | 285          |
| NA                              | 81           |
| Vital status                    |              |
| Alive                           | 289          |
| Deceased                        | 212          |
| NA                              | 6            |

NA, data unavailable; tumor; N, node; M, metastasis.
Assessment of the prognostic values of prognostic risk scores in the validation and universal sets. The three prognosis-associated DELs were validated in the validation and universal sets (including the test set and the validation set). In the validation set (P=0.0014; Fig. 6A) and the universal set (P<0.0001; Fig. 6B), the OS of patients in the high risk group was significantly decreased compared with the low risk group. Additionally, the ROC curves illustrated that the prognostic risk scores of the three prognosis-associated DELs were able to predict the 5-year survival of patients in the validation set (AUC, 0.61; Fig. 6C) and the universal set (AUC, 0.63; Fig. 6D). Though the AUCs of the
Figure 3. ROC curves and KM curves of the three prognosis-associated differentially expressed IncRNAs in lung squamous cell carcinoma samples and adjacent samples of the test set. (A) RP5-821D11.7 ROC curve, (B) APCDD1L-AS1 ROC curve, (C) RP11-277P12.9 ROC curve, (D) RP5-821D11.7 KM curve, (E) APCDD1L-AS1 KM curve and (F) RP11-277P12.9 KM curve. AUC, area under the curve; OS, overall survival; CI, confidence interval; ROC, receiver operating characteristic; KM, Kaplan-Meier.
**Table II.** Cox univariate regression analysis between prognostic risk scores/clinical characteristics and overall survival of patients.

| Risk scores/clinical characteristics | Hazard ratio | Lower.95  | Upper.95 | P-value |
|--------------------------------------|--------------|-----------|----------|---------|
| Risk score                           | 2.718        | 1.720     | 4.297    | <0.001  |
| Neoplasm recurrence                  | 2.479        | 1.594     | 3.856    | <0.001  |
| TNM stage                            | 2.254        | 1.402     | 3.625    | <0.001  |
| Tobacco smoking history              | 0.633        | 0.421     | 0.951    | 0.028   |
| M stage                              | 3.637        | 1.137     | 11.635   | 0.030   |
| T stage                              | 1.663        | 1.030     | 2.686    | 0.038   |
| Target molecular therapy             | 0.689        | 0.409     | 1.160    | 0.161   |
| Residual tumor                       | 1.215        | 0.821     | 1.799    | 0.331   |
| Radiotherapy                         | 1.349        | 0.731     | 2.489    | 0.338   |
| N stage                              | 1.188        | 0.781     | 1.806    | 0.421   |
| Gender                               | 1.200        | 0.744     | 1.935    | 0.455   |
| Age                                  | 1.016        | 0.671     | 1.538    | 0.939   |

T, tumor; N, node; M, metastasis.

ROCs predicting 5-year survival were small (0.61 and 0.63; Fig. 6C and D), the KM curves did illustrate an association between the three DEL-signature and survival (P=0.0014 and P<0.0001; Fig. 6A and B).

**Functional analysis of important lncRNAs.** Using the MEM online tool and STRING database, co-expression genes of **RP5-821D11.7** [including proliferating cell nuclear antigen (**PCNA**)], **APCDDIL-ASI** [including semaphorin 5A (**SEMA5A**), semaphorin 6D (**SEMA6D**), ADAMTS like 1 (**ADAMTSL1**), ADAM metallopeptidase with thrombospondin type 1 motif 6 (**ADAMTS6**), slit guidance ligand 3 (**SLIT3**) and tenascin-C (**TNC**)] and **RP11-277P12.9** [including Wnt family member 2B (**WNT2B**) were screened. Enrichment analysis demonstrated that only the co-expression genes of **APCDDIL-ASI** were enriched in certain GO terms and KEGG pathways (Table IV). Notably, ‘positive regulation of cell migration’ (P=0.048, involving **SEMA5A** and **SEMA6D**) and ‘proteinaceous extracellular matrix’ (P=0.017, involving **ADAMTSL1** and **ADAMTS6**) were enriched.

**Discussion**

In the present study, a total of 2,041 significant DELs between LUSC and adjacent samples were identified. A prognostic risk model involving three prognosis-associated DELs (including **RP5-821D11.7**, **APCDDIL-ASI** and **RP11-277P12.9**) was established. The prognostic risk scores were able to predict the 5-year survival of patients to a certain degree, indicating that the classification effect of the prognostic risk model was good.
Cox multivariate regression analysis suggested that only prognostic risk score and tobacco smoking history had the potential to be used as independent prognostic factors. Besides, the prognostic risk model was validated in the validation set and the universal set. In addition, certain co-expression genes of RP5-821D11.7 (including PCNA), APCDD1L-AS1 (including **Table III.** Cox multivariate regression analysis between prognostic risk scores/clinical characteristics and overall survival of patients.

| Risk scores/clinical characteristics | Hazard ratio | Lower.95 | Upper.95 | P-value |
|--------------------------------------|-------------|----------|----------|---------|
| Risk score                           | 3.747       | 1.765    | 7.957    | <0.001  |
| Tobacco smoking history              | 0.585       | 0.344    | 0.995    | 0.048   |
| Neoplasm recurrence                  | 1.486       | 0.871    | 2.535    | 0.146   |
| M stage                              | 3.026       | 0.550    | 16.640   | 0.203   |
| TNM stage                            | 1.711       | 0.658    | 4.451    | 0.271   |
| T stage                              | 0.838       | 0.325    | 2.161    | 0.714   |

T, tumor; N, node; M, metastasis.

Figure 5. Correlation between prognostic risk scores and other clinical characteristics. Receiver operating characteristic curves demonstrating that prognostic risk scores had a degree of correlation with (A) distant metastasis, (B) tumor recurrence and (C) residual tumor. AUC, area under the curve.
**SEMA5A, SEMA6D, ADAMTSL1, ADAMTS6, SLIT3 and TNC** and RP11-277P12.9 (including WNT2B) were screened. The SLIT/ROBO signaling pathway acts by regulating tumor cell metastasis, and **SLIT3** serves as a promising tumor suppressor gene in lung adenocarcinoma (LAD) (30,31). The expression of TNC, S100A10 and S100A11 may predict survival in patients with LAD, indicating that these factors may be promising markers for better diagnosis and therapy in LAD (32,33). TNC expression is markedly elevated in patients with NSCLC, implying that **TNC** may serve as a prognostic marker for NSCLC (34,35). Semaphorins are a large number of transmembrane, glycosylphosphatidylinositol-linked and secreted proteins that are able to suppress and promote tumors (36). Downregulated **SEMA5A** is correlated with poor survival in patients with NSCLC, thus **SEMA5A** may be a prognostic marker for the disease (37). In the present study, enrichment analysis suggested that **SEMA5A** and **SEMA6D** were enriched in ‘positive regulation of cell migration’. These results indicated that **APCDD1L-AS1** may affect the prognosis of LUSC by affecting the expression levels of **SEMA5A**, **SEMA6D**, **SLIT3** and **TNC**.

Functional enrichment analysis demonstrated that **ADAMTSL1** and **ADAMTS6** were enriched in ‘proteinaceous extracellular matrix’. The ADAMTS enzymes are zinc metalloendopeptidases that affect the structure and function of the extracellular matrix (ECM) (38). **ADAMTSL-1** belongs to the

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Figure 6. Assessment of the prognostic values of prognostic risk scores in the validation and universal sets. Kaplan-Meier curves indicating that the OS of patients in the high risk group was significantly decreased for (A) the validation set and (B) the universal set, and receiver operating characteristic curves demonstrating that the three prognosis-associated differentially expressed long non-coding RNAs were able to predict the 5-year survival of patients in (C) the validation set and (D) the universal set. OS, overall survival; AUC, area under the curve.
family of ADAMTS-like proteins and may serve important roles in the ECM (39). The ECM is important in mesenchymal cancer cells; in particular, its compositional and structural alterations may affect metastasis of mesenchymal lung cancer cells (40). Dysregulation of certain ADAMTS proteinases may be directly implicated in tumor development and metastasis (41). Therefore, 

APCDD1L-AS1 may be associated with the prognosis of LUSC through ADAMTSL1 and ADAMTS6.

A previous study reported that PCNA is specifically targeted by miR-363-3p, and may inhibit tumor growth in LAD (42). PCNA may be inhibited by the small molecule AOH1160, which suppresses the growth of SCLC cells without inducing any unacceptable side-effects and may be used as a potential anticancer therapy (43). Dysregulated Wnt signaling functions in the progression and metastasis of lung cancer, and inhibitors of WNT signaling are promising for the treatment of the disease (44,45). WNT2 may promote NSCLC cell growth by activating the Wnt/β-catenin signaling pathway, suggesting that WNT2 may be a marker for the diagnosis and prognosis of NSCLC (46). Thus, RP5-821D11.7 (co-expressed with PCNA) and RP11-277P12.9 (co-expressed with WNT2B) may be used for predicting the prognosis of LUSC.

There are certain limitations to the present study. First, these findings resulted from bioinformatics analysis and require further validation. Since the sample and experimental conditions are insufficient, it is not possible to perform verification experiments at present. Furthermore, it was identified from the Cox univariate regression analysis that only neoplasm recurrence, risk score and T stage were associated with the overall survival of patients. Therefore, only these three indicators were included in the Cox multivariate regression analysis, and only neoplasm recurrence and risk score were associated with the overall survival of patients. It was hypothesized that this may result from the relatively small sample size and its unbalanced distribution. For example, the number of patients with T3 and T4 stages was significantly lower compared with T1 and T2 stages. Similarly, the number of patients with N2-N3 stages was significantly lower compared with N0 and N1 stages. In

| Category          | Term                                      | P-value | Genes                  |
|-------------------|-------------------------------------------|---------|------------------------|
| Pathway           | Axon guidance                             | <0.001  | SEMA5A, SEMA6D, NTNG1, NFATC4, SLIT3 |
|                   | ECM-receptor interaction                   | 0.013   | TNC, COL6A3, ITGA11    |
|                   | Olfactory transduction                     | 0.043   | OR4C13, OR5J2, OR1L6, OR8H2 |
| Biological process| Cell adhesion                             | <0.001  | NRP2, SEMA5A, COL7A1, TNC, COL6A3, ITGA11, COL8A1 |
|                   | Negative chemotaxis                        | <0.001  | NRP2, SEMA5A, SEMA6D, SLIT3 |
|                   | Extracellular matrix organization          | <0.001  | COL7A1, TNC, COL6A3, ITGA11, COL8A1 |
|                   | Semaphorin-plexin signaling pathway        | 0.002   | SEMA5A, PLXNA4, SEMA6D |
|                   | Collagen catabolic process                 | 0.007   | COL7A1, COL6A3, COL8A1 |
|                   | Proteolysis                                | 0.014   | CPA4, ADAMTS6, ADAMTS1, PAPPA2, HTRA3 |
|                   | Facial nerve structural organization       | 0.017   | NRP2, PLXNA4            |
|                   | Axon extension involved in axon guidance   | 0.023   | NRP2, SLIT3             |
|                   | Detection of chemical stimulus involved in sensory perception of smell | 0.046   | OR4C13, OR5J2, OR1L6, OR8H2 |
|                   | Heart development                          | 0.047   | NRP2, FOXL1, NFATC4     |
|                   | Positive regulation of cell migration      | 0.048   | SEMA5A, SEMA6D, LRPC15  |
|                   | Negative regulation of axon extension      | 0.048   | SEMA5A, SEMA6D          |
| Cellular component| Extracellular matrix                       | 0.003   | COL7A1, TNC, COL6A3, COL8A1, SSC5D |
|                   | Endoplasmic reticulum lumen                | 0.007   | ADAMTS1, COL7A1, COL6A3, COL8A1 |
|                   | Extracellular region                       | 0.014   | NRP2, PTHLH, COL7A1, TNC, COL6A3, PAPPA2, HTRA3, COL8A1, SLIT3 |
|                   | Proteinaceous extracellular matrix         | 0.017   | ADAMTS6, ADAMTS1, COL6A3, SLIT3 |
| Molecular function| Semaphorin receptor complex                | 0.022   | NRP2, PLXNA4             |
|                   | Metalloproteinase activity                 | 0.010   | ADAMTS6, ADAMTS1, PAPPA2 |
|                   | Syndecan binding                           | 0.011   | SEMA5A, TNC              |
|                   | Semaphorin receptor activity               | 0.023   | NRP2, PLXNA4             |
|                   | Semaphorin receptor binding                | 0.043   | SEMA5A, SEMA6D           |
|                   | Laminin binding                            | 0.046   | LRPC15, SSC5D            |
|                   | Olfactory receptor activity                | 0.047   | OR4C13, OR5J2, OR1L6, OR8H2 |
|                   | Fibronectin binding                        | 0.048   | LRPC15, SSC5D            |
|                   | Chemorepellent activity                    | 0.050   | SEMA5A, SEMA6D           |

Table IV. The Gene Ontology terms and pathways enriched for the co-expression genes of APCDD1L-AS1.
addition, only seven patients were M1, while 411 patients were M0. However, the present prognosis risk model may be a valuable tool for further research. In conclusion, a total of 2,041 significant DELs were identified in LUSC samples. *RP5-821D11.7* (co-expressed with *PCNA*), *APCDDIL-AS1* (co-expressed with *SEMA5A, SEMA6D, ADAMTS5L1, ADAMTS56, SLIT3* and *TNC*) and *RP11-277P12.9* (co-expressed with *WNT2B*) may be important lncRNAs associated with the prognosis of LUSC.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

ZW conceived and designed the study. YL and ZX designed and performed data analyses. XZ collected the data and wrote the manuscript. PZ provided critical suggestion and organized the literature. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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