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Aberrant expressed long non-coding RNAs in laryngeal squamous-cell carcinoma

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ABSTRACT

Purpose: Laryngeal squamous-cell carcinoma (LSCC) is the second most common malignant tumor of head and neck squamous cell carcinoma. The study was aimed to identify key long non-coding RNAs (lncRNAs) biomarkers for LSCC.

Methods: Differentially expressed lncRNAs (DElncRNAs) and mRNAs (DEmRNAs) between LSCC and adjacent tissues were obtained based on The Cancer Genome Atlas. DElncRNA-DEmRNAs co-expression and DElncRNA-nearby-target DEmRNA interaction networks were constructed. Receiver operating characteristic and survival analysis were performed. A published dataset were as used to validate the result of bioinformatics analysis.

Results: We obtained 1103 DEmRNAs and 306 DElncRNAs between LSCC and adjacent tissues. A total of 338 DElncRNA-DEmRNA co-expression pairs and 229 DElncRNA-nearby-target DEmRNA pairs were obtained. Ten DElncRNAs and six DEmRNAs has great diagnostic value for LSCC. HOXB9 has potential prognostic value for LSCC. The results of GSE84957 validation were generally consistent with our results.

Conclusion: Our study provided clues for understanding the mechanism and developing potential biomarkers for LSCC.

1. Introduction

As the second most common malignant tumor of head and neck squamous cell carcinoma (HNSC), laryngeal squamous cell carcinoma (LSCC) represents about 2.4% of all cancer cases and 2.1% of all cancer deaths worldwide [1,2]. Although the treatment for LSCC including surgery, radiotherapy, chemotherapy and concurrent chemo-radiotherapy has developed the survival of patients with LSCC, the LSCC-related mortality remains high [3]. Moreover, the mechanism of the occurrence and development of LSCC remains unclear. Hence, it is essential to explore the mechanism of LSCC and developing novel diagnose biomarkers and therapeutic target for LSCC.

Long-noncoding RNAs (lncRNAs) are a class of RNA molecules defined as transcripts longer than 200 nucleotides that lack protein coding potential which could significantly regulate gene expression and affect cellular processes by interaction with DNA, RNA, or protein molecules [4,5]. Recent years, accumulated evidence indicated that lncRNAs could play crucial roles in the mechanism of various cancers and serve as potential diagnostic and prognostic biomarkers and therapeutic targets [6–9]. Several lncRNAs such as HOTAIR, H19 and NEAT1 have been reported to involve with LSCC [10–12].

In this present study, we obtained the lncRNA and mRNA expression profile between LSCC and adjacent tissues from The Cancer Genome Atlas (TCGA). Based on bioinformatics analysis, differentially expressed lncRNAs (DElncRNAs) and mRNAs (DEmRNAs) between LSCC and adjacent tissues were obtained. Functional annotation of DEmRNAs interacted with DElncRNAs provided clues for the functions of DElncRNAs in LSCC. Receiver operating characteristic (ROC) and survival analysis made contribution for developing potential diagnostic and prognostic value for LSCC.

2. Materials & methods

2.1. mRNA and lncRNA profiles of LSCC in TCGA

The Cancer Genome Atlas (TCGA) is a comprehensive database that consisted of multidimensional data of various cancers at DNA, RNA and protein levels. In this present study, the clinical information of patients

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Table 1
The top 10 up- and down-regulated DElncRNAs between LSCC and adjacent tissues.

Ensembl gene ID	Symbol	log2Fold change	*p*-Value	Regulation
ENSG00000227028	SLC8A1-AS1	−6.330188411	6.29E−45	Down
ENSG00000244040	IL12A-AS1	−5.225574847	3.21E−38	Down
ENSG00000272081	CTD-2376I4.2	−3.445163228	5.24E−32	Down
ENSG00000271926	CTD-2376I4.1	−3.700263723	7.28E−32	Down
ENSG00000250073	RP11-677 M14.3	−3.385499514	1.88E−26	Down
ENSG00000228789	HCG22	−6.354747965	4.98E−18	Down
ENSG00000258616	RP11-369C8.1	−7.811517574	2.56E−16	Down
ENSG00000230825	AC005532.5	−5.126019176	1.74E−15	Down
ENSG00000269318	AC007292.3	−2.056417325	2.85E−15	Down
ENSG00000251615	RP11-774O3.3	−2.415046198	2.85E−15	Down
ENSG00000248554	RP11-159F24.6	3.392787615	4.79E−18	Up
ENSG00000257636	RP11-1103G16.1	6.423668988	9.32E−16	Up
ENSG00000229618	AC011288.2	4.879474819	1.08E−15	Up
ENSG00000250874	CTC-480C2.1	6.481264021	7.36E−14	Up
ENSG00000258053	CTD-2021H9.3	5.661199751	2.01E−13	Up
ENSG00000250920	RP11-297P16.4	7.298124357	6.51E−13	Up
ENSG00000267284	RP11-397A16.1	3.544494176	8.06E−13	Up
ENSG00000259807	RP11-426C22.4	4.234740478	1.95E−12	Up
ENSG00000249001	RP11-742B18.1	3.995137424	3.56E−12	Up
ENSG00000250133	HOXC-AS2	3.436056946	4.17E−12	Up

Table 2
The top 10 up- and down-regulated DEmRNAs between LSCC and adjacent tissues.

Ensembl gene ID	Symbol	log2Fold change	*p*-Value	Regulation
ENSG00000114166	KAT2B	−2.825122061	3.02E−29	Down
ENSG00000134531	EMP1	−4.024808312	1.02E−26	Down
ENSG00000157107	FCHO2	−2.34782862	2.00E−24	Down
ENSG00000145916	RMND5B	−2.056551632	1.61E−23	Down
ENSG00000122042	UBL3	−2.177827695	2.49E−23	Down
ENSG00000125733	TRIP10	−2.241638248	3.98E−23	Down
ENSG00000214097	SMCO1	−6.194602235	7.40E−22	Down
ENSG00000181830	SLC35C1	−2.078082654	1.05E−21	Down
ENSG00000106351	AGFG2	−2.537259048	1.98E−21	Down
ENSG00000250878	METTL21EP	−5.854011742	2.32E−21	Down
ENSG00000164283	ESM1	4.685762838	2.13E−27	Up
ENSG00000139800	ZIC5	6.012818666	1.02E−26	Up
ENSG00000187498	COL4A1	3.241858921	6.63E−24	Up
ENSG00000128713	HOXD11	5.274347109	1.21E−23	Up
ENSG00000134871	COL4A2	3.009790208	9.68E−23	Up
ENSG00000123364	HOXC13	4.807297856	9.66E−22	Up
ENSG00000173157	ADAMTS20	7.427918525	3.45E−20	Up
ENSG00000128710	HOXD10	4.056226554	7.16E−20	Up
ENSG00000134668	SPOCD1	3.8526257	3.06E−19	Up
ENSG00000162849	KIF26B	3.578040469	4.05E−19	Up

with HNSC was downloaded from TCGA (http://tcga-data.nci.nih.gov/). Among them, patients with LSCC who has no history of malignancy and neoadjuvant treatment were enrolled in this study. The Mrna and lncRNA expression profile between LSCC and adjacent tissues were downloaded from TCGA (http://tcga-data.nci.nih.gov/).

2.2. DEmRNAs and DElncRNAs in LSCC compared to adjacent tissues

Both DEmRNAs and DElncRNAs in LSCC compared to adjacent tissues were calculated via R-bioconductor package DESeq. The threshold for both the DEmRNAs and DElncRNAs was FDR < 0.0001 and |log2(Fold change) normalized| > 2.

2.3. LSCC-specific DElncRNA-DEmRNA co-expression network

Firstly, pairwise Pearson correlation coefficients between DEmRNAs and DElncRNAs were calculated. DElncRNA-DEmRNA pairs with *p*-value < 0.01 and |r| > 0.95 were served as significant DElncRNA-DEmRNA co-expression pairs. Based on these DElncRNA-DEmRNA co-expression pairs, the DElncRNA-DEmRNA co-expression network was constructed and visualized by using Cytoscape Software (http://www.cytoscape.org/).

2.4. Nearby-target DEmRNAs of DElncRNAs in LSCC

To identify the target DEmRNAs of DElncRNAs by cis-regulatory effects, the DEmRNAs transcribed within a 100 kb window up- or downstream of DElncRNAs were searched which were defined as nearby cis target DEmRNAs of DElncRNAs.

2.5. Functional annotation

Both DEmRNAs co-expressed with DElncRNAs and nearby-target DEmRNAs of DElncRNAs were served as DEmRNAs interacted with DElncRNAs. To better research the functions of DElncRNAs in LSCC, functional annotation including Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis of DEmRNAs interacted with DElncRNAs were performed by using String (https://string-db.org/). KEGG pathway enrichment analysis of all the DEmRNAs between LSCC and adjacent tissues were performed by using String (https://string-db.org/) as well.

2.6. Receiver operating characteristic (ROC) analyses

By using pROC package in R language, we performed receiver operating characteristic (ROC) analyses to assess the diagnostic value of selected DElncRNAs and DEmRNAs. Area under the curve (AUC) within binomial exact confidence interval was calculated and ROC curve was generated.

2.7. Survival analysis of DEmRNAs in LSCC

By using the survival (https://cran.r-project.org/web/packages/survival/index.html) in R, we analyzed the association between DEmRNAs and survival in patients with LSCC. Due to restrictions of TCGA, we did not perform survival analysis of DElncRNAs in LSCC.

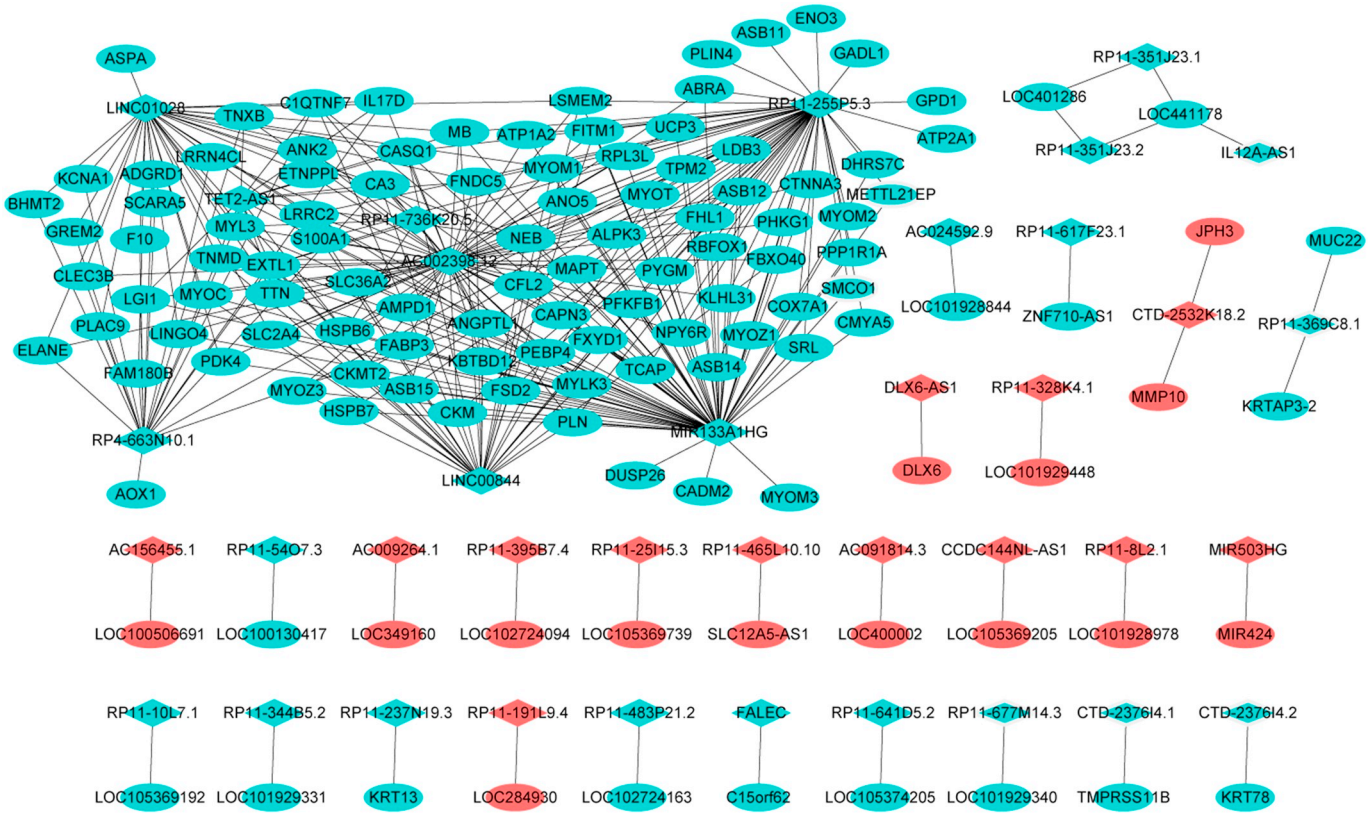

Fig. 1. LSCC-specific DElncRNA-DEmRNA co-expression network.
Rhombus and ellipse represented DElncRNAs and DEmRNAs, respectively.
Red and blue color represented up- and down-regulation, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2.8. Validation in the Gene Expression Omnibus (GEO) dataset

GSE84957 dataset was downloaded from the GEO (https://www.ncbi.nlm.nih.gov/geo/), which consisted of 9 patients with LSCC and 9 normal controls. The dataset GSE84957 examined the tissue sample, which was all from China. The expression pattern of selected DEmRNAs and DElncRNAs were validated with GSE84957 datasets.

3. Results

3.1. mRNAs and lncRNAs expression profile of LSCC derived from TCGA

Data of a total of 528 patients with HNSC were downloaded from TCGA data portal. Among them, there is 105 patients with LSCC who has no history of malignancy and neoadjuvant treatment were enrolled in this study. The mRNA and lncRNA expression profile (UNC IlluminaHiseq_RNASeqV2) of 105 patients with LSCC and 9 adjacent tissues were downloaded. The majority of patients were male (81.90%) and female account for 18.10%. The stage of patients were stage I (1.90%), stage II (8.57%), stage III (11.43%), stage IV (65.71%). The stage of 12.38% patients was not available. The race of patients was white (77.14%), Black or African American (18.10%), American Indian or Alaska native (1.00%) Asian (1.00%).

3.2. DEmRNAs and DElncRNAs between LSCC and adjacent tissues

A total of 1103 DEmRNAs (391 down-regulated and 712 up-regulated DEmRNAs) and 306 DElncRNAs (107 down-regulated and 199 up-regulated DElncRNAs) between LSCC and adjacent tissues were obtained. The top 10 up- and down-regulated DElncRNAs and DEmRNAs between LSCC and adjacent tissues were displayed in Tables 1 and 2, respectively.

3.3. LSCC-specific DElncRNA-DEmRNA co-expression network

A total of 338 DElncRNA-DEmRNA co-expression pairs were obtained with p-value < 0.01 and $|r| > 0.95$. The DElncRNA-DEmRNA co-expression network was consisted of 162 nodes and 338 edges. MIR133A1HG (degree = 72), AC002398.12 (degree = 61) and RP11-255P5.3 (degree = 60) were three hub lncRNAs of the LSCC-specific DElncRNA-DEmRNA co-expression network (Fig. 1). MYLK3, was a shared DEmRNA co-expressed with both MIR133A1HG and RP11-255P5.3. TNXB was a co-expressed DEmRNA with AC002398.12.

3.4. Nearby-target DEmRNAs of DElncRNAs in LSCC

A total of 229 DElncRNA-nearby-target DEmRNA pairs including (131 DElncRNAs and 167DEmRNAs) in LSCC were obtained. The LSCC-

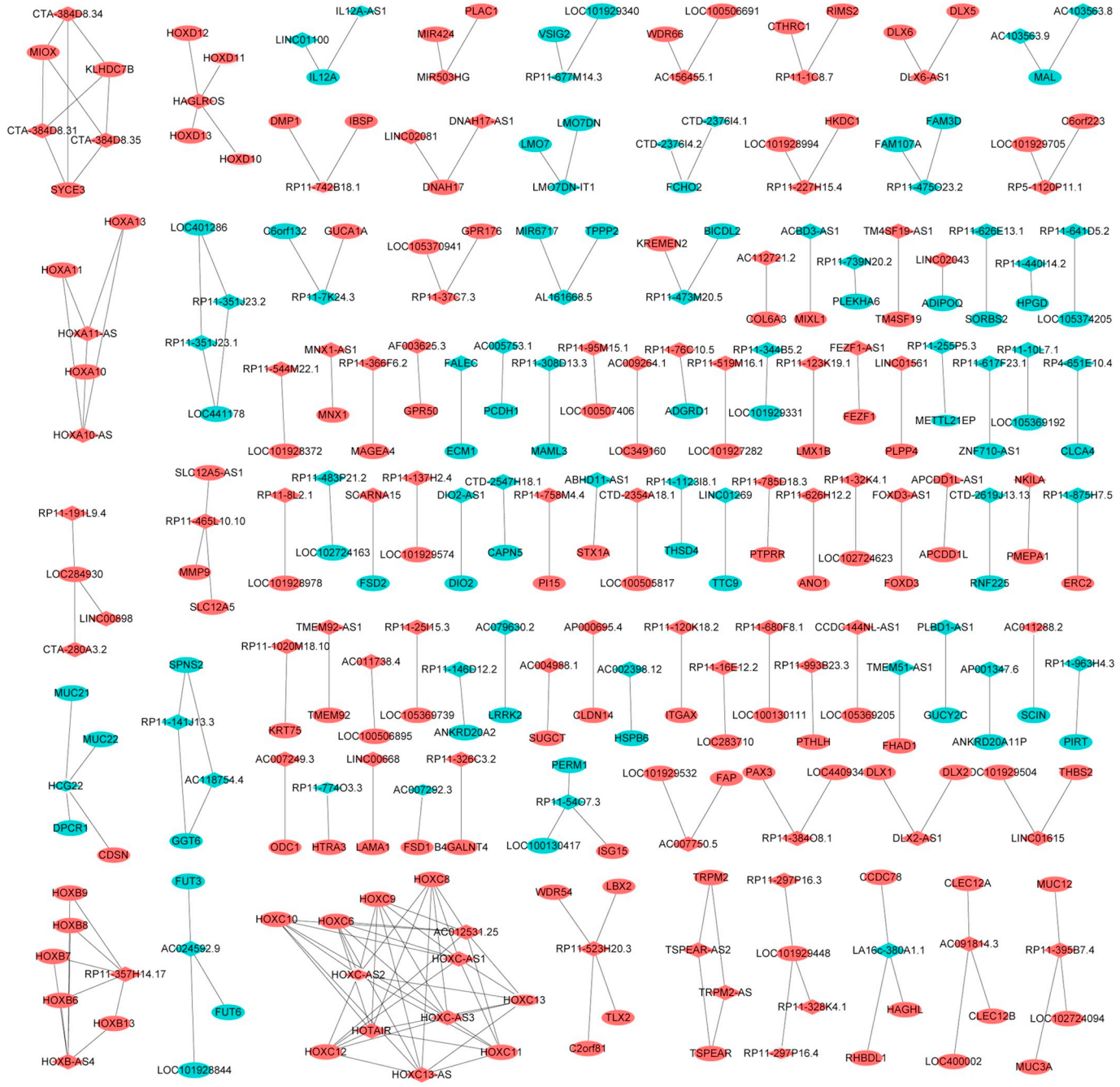

Fig. 2. LSCC-specific DElncRNA-nearby-target DEmRNA interaction network. Rhombus and ellipse represented DElncRNAs and DElncRNAs, respectively. Red and blue color represented up- and down-regulation, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

specific DElncRNA-nearby-target DEmRNA interaction network was consisted of 296 nodes and 229 edges. HOXC-AS1 (degree = 7), HOXC-AS2 (degree = 7), HOTAIR (degree = 7), HOXC13-AS (degree = 7) were four hub DElncRNAs (Fig. 2).

HOXC-AS1/HOXC-AS2/HOXC-AS3/HOTAIR/HOXC13-AS/AC012531.25-HOXC13/HOXC8, HAGLROS-HOXD11/HOXD10 and RP11-357H14.17/HOXB-AS4-HOXB9/HOXB13 were several identified DElncRNA-nearby-target DEmRNA pairs.

3.5. Functional annotation of DEmRNAs in LSCC

Based on the functional annotation of all the 1103 DEmRNAs in LSCC (Table 3), focal adhesion was a significantly enriched pathway in

Table 3
Significantly enriched pathways of DEmRNAs between LSCC and adjacent tissues.

KEGG ID	Pathway description	Counts	FDR	Enriched genes
4512	ECM-receptor interaction	18	3.24E−05	COL11A1, COL24A1, COL27A1, COL4A1, COL4A2, COL4A5, COL4A6, COL5A2, COL6A3, FN1, IBSP, LAMA1, LAMC2, SPP1, THBS2, TNC, TNN, TNXB
5146	Amoebiasis	18	0.000372	COL11A1, COL24A1, COL27A1, COL4A1, COL4A2, COL4A5, COL4A6, COL5A2, CSF2, FN1, GNA14, IL12A, IL8, LAMA1, LAMC2, SERPINB1, SERPINB13, SERPINB2
4510	Focal adhesion	25	0.00172	COL11A1, COL24A1, COL27A1, COL4A1, COL4A2, COL4A5, COL4A6, COL5A2, COL6A3, FN1, IBSP, LAMA1, LAMC2, MYL7, MYLK3, MYLK4, MYLPF, PGF, PPP1R12B, RASGRF1, SPP1, THBS2, TNC, TNN, TNXB
4974	Protein digestion and absorption	13	0.0132	ATP1A2, COL11A1, COL13A1, COL22A1, COL24A1, COL27A1, COL4A1, COL4A2, COL4A5, COL4A6, COL5A2, COL6A3, CPA2
5323	Rheumatoid arthritis	13	0.0132	ATP6V0A4, CCL20, CD80, CSF2, CTLA4, CXCL5, FOS, IL11, IL8, MMP1, MMP3, TNFRSF11A, TNFSF11
3320	PPAR signaling pathway	11	0.0199	ADIPOQ, AQP7, CYP8B1, FABP3, FADS2, MMP1, OLR1, PLIN1, SCD5, SLC27A6, SORBS1

FDR, false discovery rate.

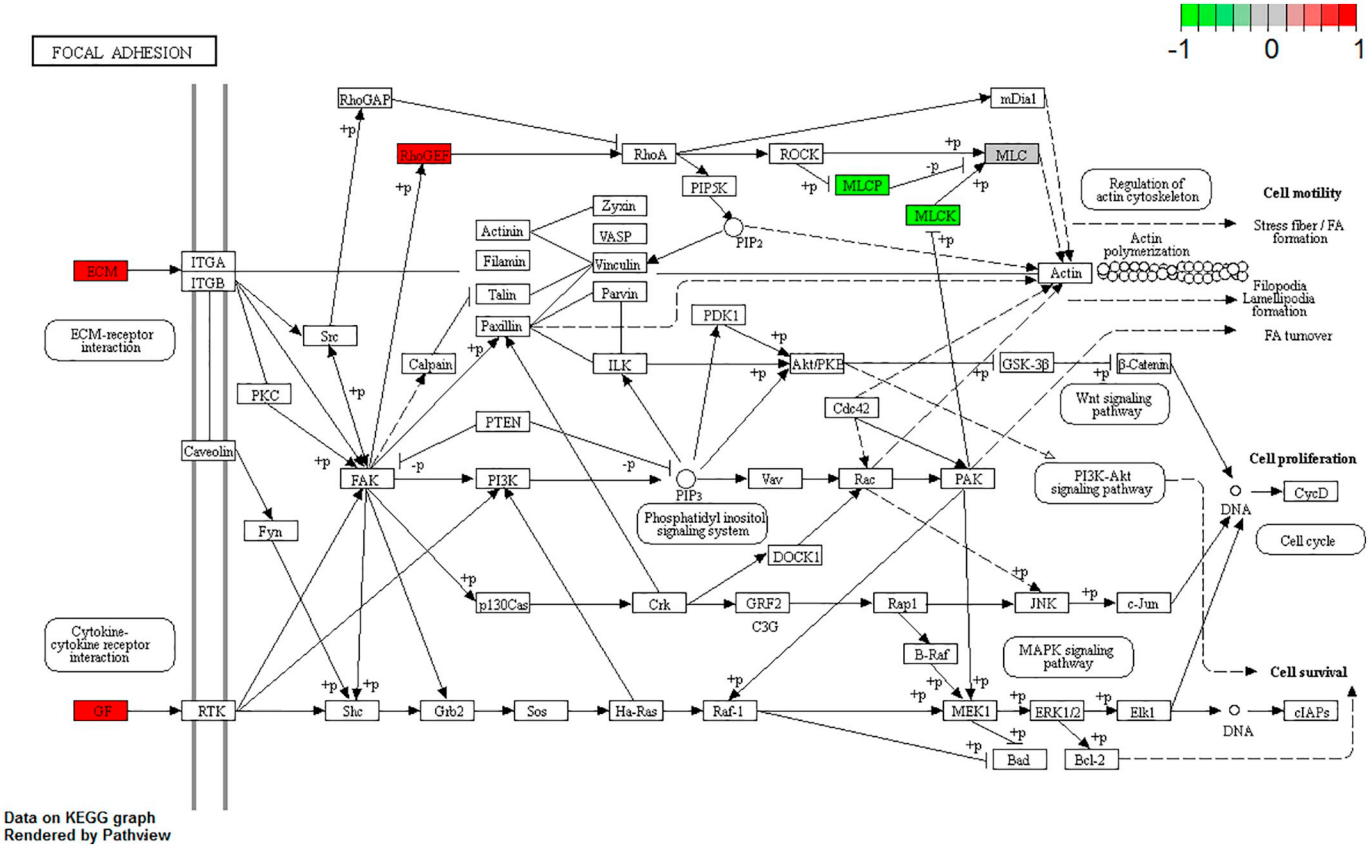

Fig. 3. Pathway of focal adhesion.
Focal adhesion was a significantly enriched pathway of DEmRNAs between LSCC and adjacent tissues. The red and green rectangles represented the particles which regulated by the up- and down-regulated DEmRNAs that enriched in pathway of focal adhesion, respectively. The red and green rectangles represent components regulated by DEmRNAs that are enriched in LSCC. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

LSCC (FDR = 1.72E−03, Fig. 3). MYLK3 and TNXB were two DEmRNAs enriched in pathway of focal adhesion.

A total of 264 DEmRNAs (149 down-regulated DEmRNAs and 115 up-regulated DEmRNAs) interacted with 139 DElncRNAs (58 down-regulated DElncRNAs and 81 up-regulated DElncRNAs) were obtained. There was no enriched pathway of these 264 DEmRNAs. Skeletal system development (FDR = 2.67E−07), structural constituent of muscle (FDR = 1.26E−06) and sarcomere (FDR = 1.30E−10) were three significantly enriched GO terms of these 264 DEmRNAs in LSCC (Fig. 4).

3.6. Receiver operating characteristic (ROC) analyses

We assess the diagnostic value of 10 DElncRNAs (HOTAIR, HCG22, HOXB-AS4, HOXC-AS1, HOXC-AS2, HOXC-AS3, HOXC13-AS, HAGLROS, AC012531.25 and RP11-357H14.17) and 6 DEmRNAs (HOXB9, HOXC8,

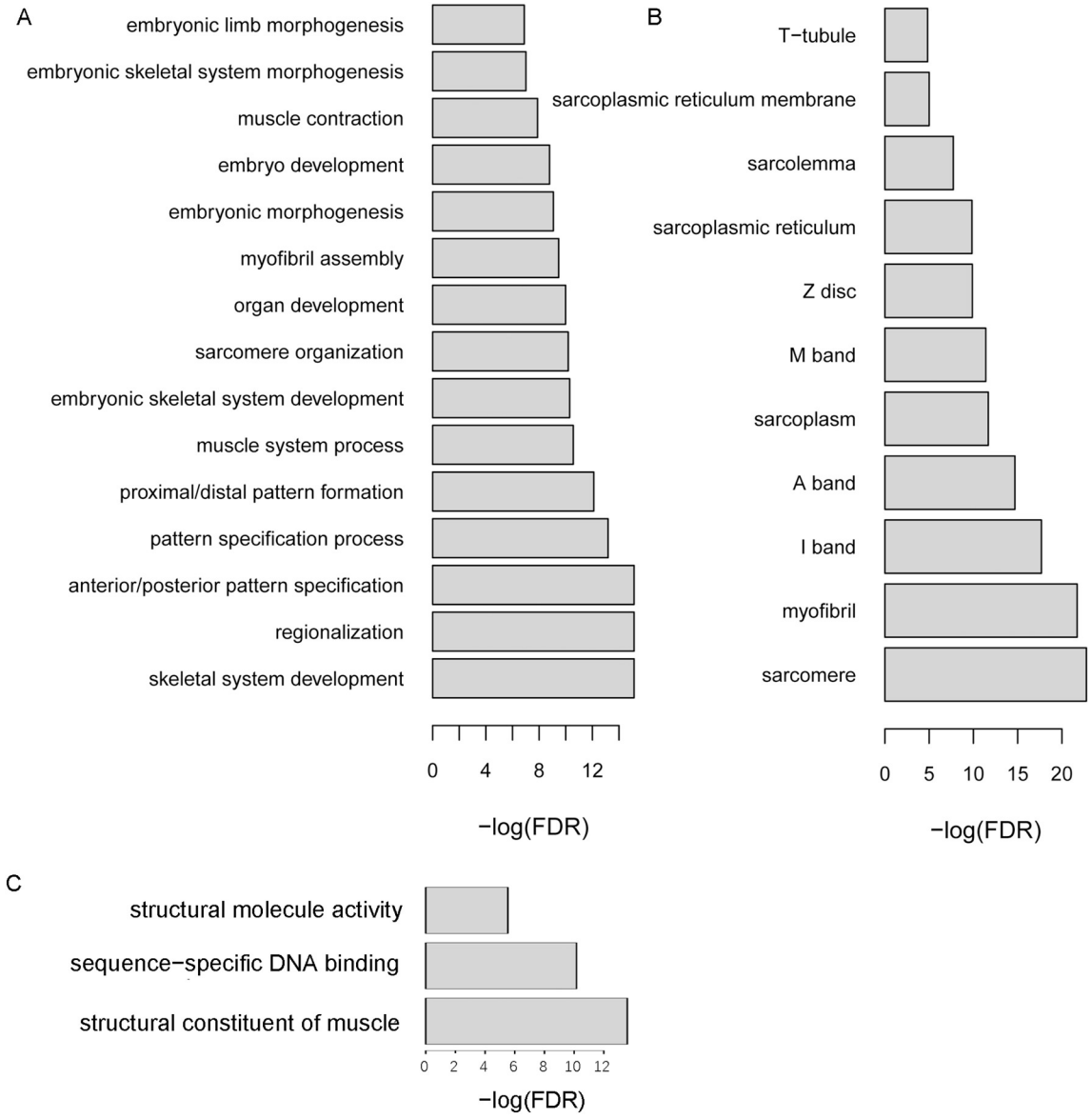

Fig. 4. Significantly enriched GO terms of DEmRNAs interacted with DElncRNAs.
The x-axis shows − log FDR and y-axis shows GO terms.
(A) Biological process; (B) cellular component; (C) molecular function.

HOXC13, HOXD10, HOXD11 and TNXB) in LSCC. The AUC of all these 10 DElncRNAs and 6 DEmRNAs was more that 0.85 (Fig. 5).

3.7. Survival analysis of DEmRNAs in LSCC

The association between 6 DEmRNAs and survival in patients with LSCC. Only HOXB9 was significantly associated with the prognosis of patients with LSCC. High expression of HOXB9 was significantly associated with lower survival rate in patients with LSCC ($p = 0.019$, Fig. 6).

3.8. Validation in the GEO dataset

The expression patterns of selected DEmRNAs (TNXB, HOXB9, S100A1, HOXC13, HOXD11, HOXB13, HOXD10, HOXC8 and MYLK3) and DElncRNAs (HOTAIR and HCG22) were verified in GSE84957

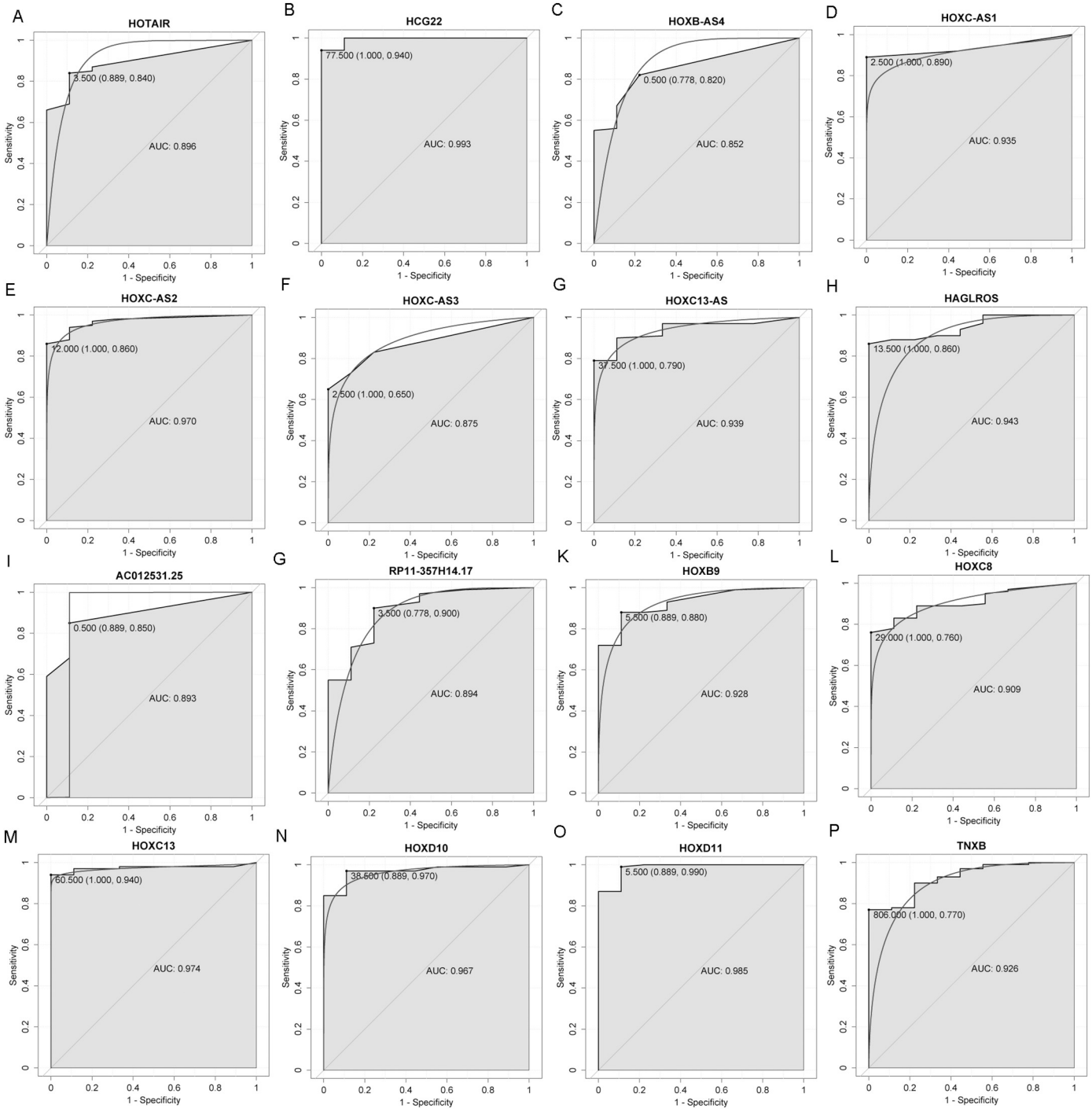

Fig. 5. ROC analysis of DElncRNAs and DEmRNAs in LSCC.
The x-axis shows 1-specificity and y-axis shows sensitivity.
A). HOTAIR; B). HCG22; C). HOXB-AS4; D). HOXC-AS1; E). HOXC-AS2; F). HOXC-AS3; G). HOXC13-AS; H). HAGLROS; I). AC012531.25; J). RP11-357H14.17; K). HOXB9; L). HOXC8; M). HOXC13; N). HOXD10; O). HOXD11; P). TNXB.

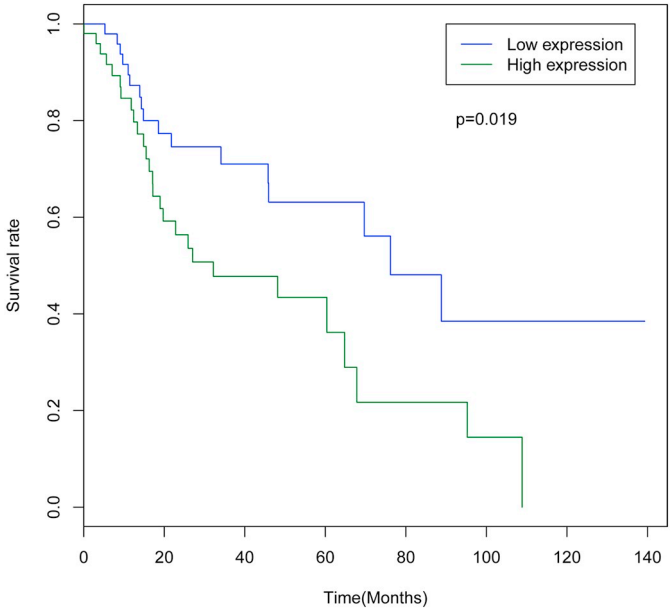

Fig. 6. Survival analysis of HOXB9 in LSCC.
The x-axis shows times (months) and y-axis shows survival rate of patients with LSCC. High expression of HOXB9 was significantly associated with lower survival rate in patients with LSCC (p = 0.019).

dataset. As shown in Figs. 7 and 8, HOXB9 and HOXB13 were down-regulated which was inconsistent with our results. However, the expression patterns of the remaining most of the selected seven mRNAs and two lncRNAs were consistent with our results. Three mRNAs (TNXB, S100A1 and MYLK3) and one lncRNA (HCG22) were down-regulated while four mRNAs (HOXC13, HOXD11, HOXD10 and HOXC8) and one lncRNA (HOTAIR) were up-regulated in LSCC, suggesting that the results were convincing.

4. Discussion

LSCC is one of the top three cancers affecting the head and neck region whose mechanism remains elusive. Accumulated studies have indicated that LncRNAs involve with various disease. Despite the fact that function of most lncRNAs remains unknown, lncRNAs have been indicated to involve with the pathogenesis of LSCC. To identify the key DElncRNAs in LSCC not only provides new clues for understanding the function of lncRNAs but also makes a contribution for developing novel biomarkers of LSCC.

Only few identified DElncRNAs between LSCC and adjacent tissues in this present study has been reported in previous studies. LincRNA HOTAIR was reported to regulate the migration and invasion of tumor cells. Over-expressed expressed HOTAIR has been found in various cancers such as LSCC, breast cancer, colorectal cancer and pancreatic cancer [3,13–15]. Up-regulated HOTAIR could not only regulate proliferation of LSCC cells but also play a crucial role in regulating the drug-resistance of LSCC cells with EZH2 serve as a key potential mediator [3]. Moreover, over-expressed HOTAIR was found to be significantly associated with T phase, pathological grades, and risk of lymphatic metastasis of LSCC [3]. In this present study, HOTAIR was also up-regulated in LSCC compared to normal controls which provided evidence for previous study. LncRNA HCG22 was found to be up-regulated in another HNSC, oral cavity and oropharyngeal squamous cell carcinoma (OSCC) which suggested its potential roles in OSCC [16]. The potential prognostic value of HCG22 was found in OSCC as well [17]. Our study firstly found the significant up-regulation of HCG22 in LSCC which suggested that HCG22 might be a potential regulator and biomarker of LSCC. Moreover, both HOTAIR and HCG22 have great diagnostic value for LSCC based on our ROC analyses.

Although the functions of lncRNAs remain largely unknown, lncRNAs was reported to play important roles in cancer biology through regulating gene expression with cis- and trans-regulatory mechanisms [18]. To better research the identified DElncRNAs in LSCC, we obtained the DEmRNAs integrated with DElncRNAs including DEmRNAs co-expressed with DElncRNAs and nearby-target DEmRNAs of DElncRNAs. Functional annotation of DEmRNAs integrated with DElncRNAs was further performed.

HOX genes have been indicated to involve with embryogenesis and regulating various biological processes such as cell differentiation, cell proliferation, and apoptosis [19]. Moreover, aberrant expressed HOX genes were associated with various cancers [20–23]. Previous studies have indicated a set of HOX genes such as HOXB9, HOXB13, HOXC13, HOXC8, HOXD10 and HOXD11 were up-regulated in LSCC tissues [23,24]. Up-regulated HOXC8 and HOXD11was associated with lower tumor differentiation and regional lymph node metastases, respectively [24]. HOXC8, HOXD10, and HOXD11 genes were reported to play critical role in cell proliferation and migration of LSCC [24]. Moreover, HOXB9 was reported to be associated with high histological grade and poor prognosis of patients with LSCC which might serve as a potential prognostic biomarker and therapeutic target in patients with LSCC [23].

In this present study, all these six HOX genes (HOXB9, HOXB13, HOXC13, HOXC8, HOXD10 and HOXD11) were up-regulated in LSCC that provided evidence for previous studies. Moreover, HOXC13 and HOXC8 were two shared nearby-target DEmRNAs of seven DElncRNAs (HOTAIR, HOXC-AS1, HOXC-AS2, HOXC-AS3, HOXC-AS4, HOXC13-AS and AC012531.25); HOXD10 and HOXD11 were two shared nearby-target DEmRNAs of lncRNA HAGLROS; HOXB9 and HOXB13 were two shared nearby-target DEmRNAs of two DElncRNAs (RP11-357H14.17 and HOXB-AS4). We speculated that these ten DElncRNAs might play key roles in LSCC by regulating the expression of HOX genes with cis-effect. Furthermore, ROC analyses in this present study revealed the diagnostic value of eight DElncRNAs (HOXC-AS1, HOXC-AS2, HOXC-AS3, HOXB-AS4, HOXC13-AS, AC012531.25, HAGLROS and RP11-357H14.17) and five DEmRNAs (HOXC8, HOXB9, HOXC13, HOXD10 and HOXD11) which might be potential biomarkers of LSCC. The potential prognostic value of HOXB9 was found based on the survival analysis in this study, as well.

Functional annotation of DEmRNAs interacted with DElncRNAs in LSCC indicated that skeletal system development, structural constituent of muscle and sarcomere were significantly enriched GO terms. Moreover, HOXB9, HOXC8, HOXD10 and HOXD11 were four genes enriched in skeletal system development. These finding provided clues for the functions of DElncRNAs in LSCC.

Based on the LSCC-specific DElncRNA-DEmRNA co-expression network, MIR133A1HG, AC002398.12 and RP11-255P5.3 were three hub lncRNAs which suggested their importance in LSCC. MYLK3, myosin light chain kinase 3 was a shared DEmRNA co-expressed with both MIR133A1HG and RP11-255P5.3. TNXB, tenascin XB was a co-expressed DEmRNA with AC002398.12 which has great diagnostic value for LSCC. Based on the KEGG enrichment analysis, both MYLK3 and

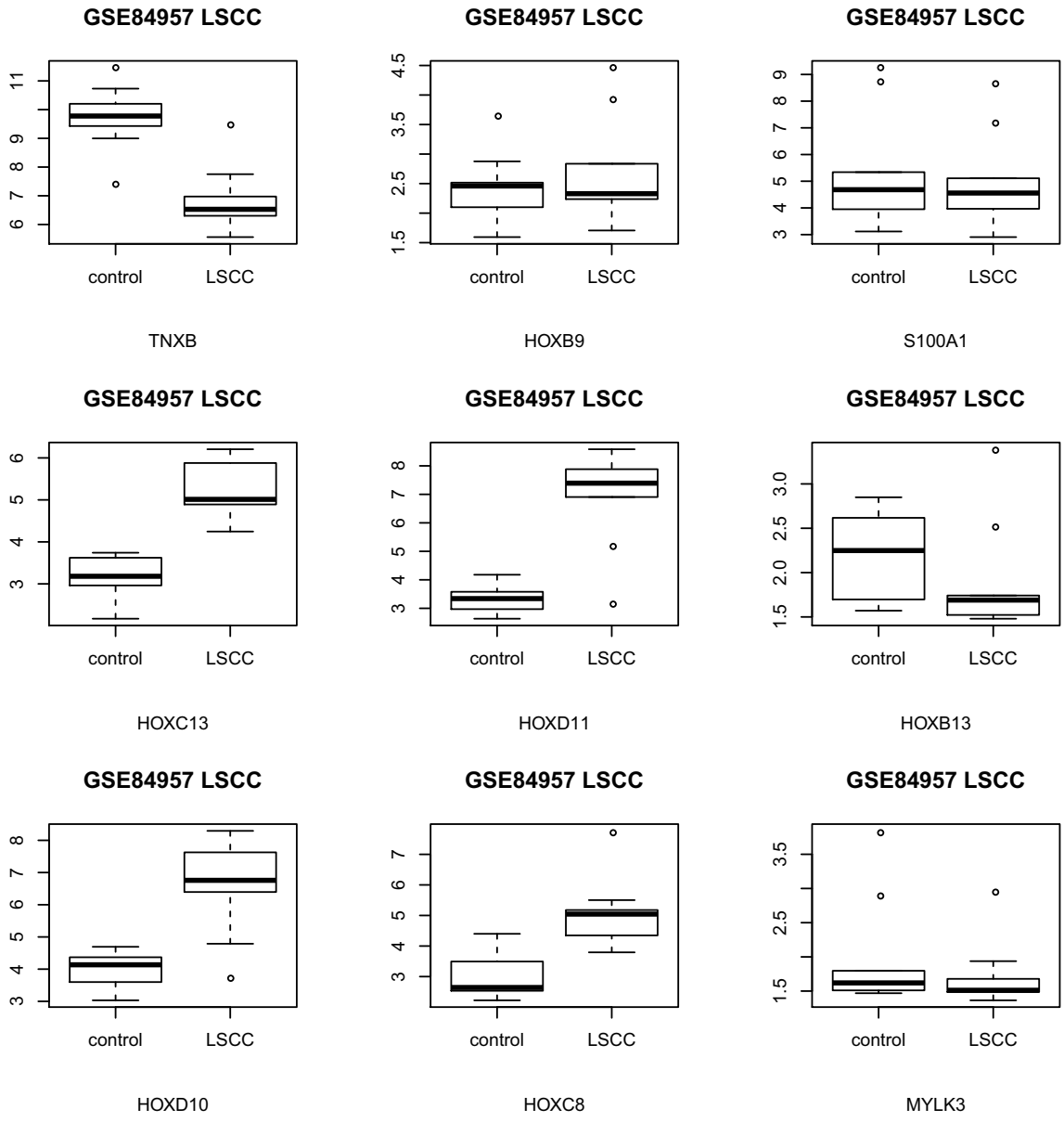

Fig. 7. Validation of selected mRNA in GSE84957.
The x-axis shows healthy normal control and LSCC groups and y-axis shows relative expression.

TNXB were genes enriched in a significantly enriched pathway in LSCC, focal adhesion. Previous studies have indicated that aberrant expression of focal adhesion kinase was associated with cellular proliferation and apoptosis of various cancers [25–27]. Aberrant focal adhesion kinase was found in patients with LSCC which might induce increased proliferation and downregulated apoptosis of LSCC cells [28]. Moreover, up-regulated focal adhesion kinase was reported be closely associated with poor survival of patients LSCC [28]. We speculated that MIR133A1HG, AC002398.12 and RP11-255P5.3 could involve with the cellular proliferation, apoptosis and prognosis of LSCC by regulating the process of focal adhesion.

5. Conclusion

In conclusion, we identified the DElncRNAs and DEmRNAs between LSCC and adjacent tissues. Our data indicated that abundant of novel DElncRNAs might be associated with the mechanism of LSCC. Function annotation of the DEmRNAs interacted with DElncRNAs contributed to exploring the functions of DElncRNAs in LSCC. Moreover, ROC and survival analysis revealed the potential diagnostic or prognostic value of key DEmRNAs and DElncRNAs for LSCC. This present study provided new clues for understanding the mechanism and developing diagnostic and therapeutic strategies of LSCC. Further experiment was needed to

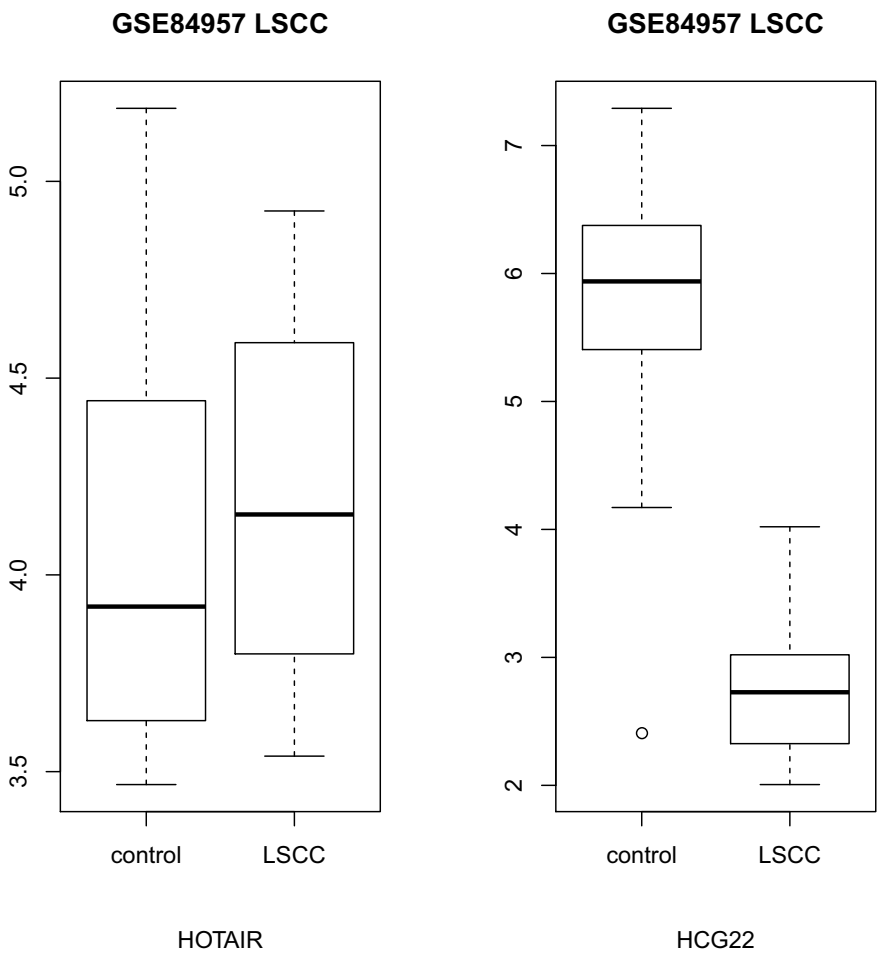

Fig. 8. Validation of selected lncRNA in GSE84957.
The x-axis shows healthy normal control and LSCC groups and y-axis shows relative expression.

explore the precise role of DElncRNAs in the pathogenesis of LSCC.

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Author contributions

Hu Li and Mei Zhang made substantial contributions to conception and design; Hu Li, Fu-Ling Wang, Wei Li and Yong-Hua Fei acquired the data; Hu Li, Fu-Ling Wang, Wei Li, Yong-Hua Fei, Ya-Ting Wang, Jing-E Zhang and Hui-Yun Bi analyzed and interpreted the data; All these authors drafted the manuscript and gave final approval of the version to be published.

Declaration of competing interest

The author reports no conflicts of interest in this work.

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