Advances in Precision Medicine, 2026, Volume 11, Issue 7
https://bbwpublisher.com/journal/APM
Online ISSN: 2424-9106
Print ISSN: 2424-8592

Long non-coding RNA LINC01123 facilitates the progression of lung cancer by targeting miR-384

Ya Zhang, Gang Cao*

Department of Respiratory Medicine, Hongze District People's Hospital, Hongze, Huai'an 223100, Jiangsu, China

Author to whom correspondence should be addressed.

Abstract: *Purpose:* Although growing evidence has demonstrated that LINC01123 plays an oncogenic role in lung cancer, the underlying mechanisms require further elucidation. *Methods:* To explore the functions of LINC01123 on cell proliferation and migration, CCK-8 and Transwell assays were performed. The relationships between LINC01123 and miR-384 were examined by luciferase reporter assays. The expression of LINC01123 and miR-384 was quantified by quantitative real-time PCR. *Results:* In this study, knockdown of LINC01123 inhibited cell proliferation and migration, while overexpression of LINC01123 enhanced these effects in lung cancer. Luciferase reporter assays verified that LINC01123 could bind directly to miR-384. Overexpression of miR-384 suppresses cell proliferation and migration. The results of the rescue experiment showed that knockdown of LINC01123 inhibited cell proliferation and migration, whereas inhibition of miR-384 counteracted the repressive effects induced by LINC01123 inhibition. *Conclusion:* Our study reveals that LINC01123 promotes lung cancer progression via miR-384 for the first time.

Keywords: Lung cancer; LINC01123; miR-384

Online publication: July 26, 2026

1. Introduction

Lung cancer remains the main cause of cancer-related deaths worldwide. Every year, approximately 2 million new patients are diagnosed with lung cancer, and 80% die [1,2]. One of the main reasons for this is the lack of effective early diagnostic strategies. Patients die from lung cancer because early diagnosis is not possible before the advanced stage of cancer [3,4]. Although various diagnostic methods for early detection, such as imaging screening, bronchoscopy, and emerging potential liquid biopsies, have made some progress, early diagnosis is still inaccurate and remains a challenge [3,5]. Therefore, exploring effective and new early diagnostic methods is crucial for improving the diagnosis and treatment of patients with lung cancer.

With the development of RNA sequencing (RNA-seq) technology, it has been revealed that only

a small fraction of RNAs, about 2%, encode proteins, and over 90% of the human genome transcribes noncoding RNAs [6]. Long noncoding RNAs (lncRNAs) are a type of RNA molecules that comprise 200 or more nucleotides with no protein-coding capacity, and have been thought to be "transcriptional noise" or "dark matter" [7,8]. Increasing evidence suggests that lncRNAs participate in the biological processes of carcinogenesis, such as growth, migration, and invasion, and some lncRNAs have been identified as diagnostic or prognostic markers for cancer [9]. In colorectal cancer, lncRNA PVT1, a novel epigenetic enhancer of MYC, is a promising risk-stratification biomarker [10]. In lung cancer, some lncRNAs promote lung cancer cell proliferation, migration, and invasion. Long intergenic non-protein coding RNA 1123 (LINC01123) has been reported to play important roles in the development and progression of multiple human cancers. However, the mechanism underlying the role of LINC01123 in lung cancer progression remains unclear.

In the present study, we found that LINC01123 expression was upregulated in lung cancer tissues and correlated with lung cancer stage. Functional experiments showed that LINC01123 promotes the proliferation and metastasis of lung cancer cells. Furthermore, molecular mechanistic studies showed that LINC01123 could directly sponge miR-384. Rescue experiments revealed that LINC01123 accelerates lung cancer cell proliferation and migration by regulating miR-384. In conclusion, our study elucidates a novel mechanism of LINC01123 in lung cancer progression and provides a potential diagnostic and therapeutic target for lung cancer patients.

2. Materials and methods

2.1. Bioinformatic analysis

Microarray analysis of the Gene Expression Omnibus (GEO) dataset (GEO: GSE101929) was performed to compare the expression levels of LINC01123 between lung cancer tissues and normal tissues. The TNMplot.com analysis platform was used to compare LINC01123 expression between tumor and normal tissues. The Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway of GSE101929 was analyzed using lnCAR software. The correlation between the expression level of LINC01123 and tumor stage was analyzed using Gene Expression Profiling Interactive Analysis (GEPIA). Primers for quantitative real-time (qPCR) detection of miRNA expression were designed using the miRNA Primer Design Tool website.

2.2. Cell culture

The human lung cell lines A549, H1975, PC9, H1299, and the human bronchial epithelial cell line HBE were obtained from the Institute of Biochemistry and Cell Biology of the Chinese Academy of Sciences (Shanghai, China). Among them, HBE, A549 and H1975 cells were cultured in 1640 medium (Thermo Fisher Scientific, Inc.), and PC9 and H1299 cells were incubated in DMEM (Thermo Fisher Scientific, Inc.). All culture media were supplemented with 10% fetal bovine serum (FBS) (Yeasen Biotechnology, Shanghai, China), 100 U/mL penicillin, and 100 mg/mL streptomycin (Thermo Fisher Scientific, Inc.). All the cells were cultured in a humidified atmosphere containing 5% CO2 at 37 ℃.

2.3. RNA extraction and quantitative real-time PCR

The cells were harvested, and total RNA was extracted using TRIzol reagent (Invitrogen, CA, USA). A PrimeScript RT kit (Takara, Dalian, China) was used to reverse transcribe 1 μg of total RNA into cDNA using

random primers. The Hifair II 1st Strand cDNA Synthesis Kit (YEASEN, Shanghai, China) was used for reverse transcription of miRNAs. The stem-loop RT primers for reverse transcription of different miRNAs, which are shown in **Table 1**, and the primers for the detection of miRNA expression were designed using the website called the miRNA Primer Design Tool. The specific primers, which are shown in **Table 2**, were designed and synthesized to detect the expression levels of different genes by quantitative real-time PCR (qPCR) using the SYBR Green Master Mix kit (Takara, Dalian, China). Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as the internal reference gene to detect mRNA expression. U6 was used as an endogenous control to detect miRNA expression. All data were calculated using the $2^{-\Delta\Delta Ct}$ method to analyze the fold changes in gene expression.

Table 1. The sequences of stem-loop RT primer

miRNA	Stem-loop RT primer
miR-34c-5p	GTTGGCTCTGGTGCAGGGTCCGAGGTATTCGCACCAGAGCCAACGCAATC
miR-384	GTTGGCTCTGGTGCAGGGTCCGAGGTATTCGCACCAGAGCCAACTATGAA
miR-876-5p	GTTGGCTCTGGTGCAGGGTCCGAGGTATTCGCACCAGAGCCAACTGGTGA
miR-449b-5p	GTTGGCTCTGGTGCAGGGTCCGAGGTATTCGCACCAGAGCCAACGCCAGC
miR-744-5p	GTTGGCTCTGGTGCAGGGTCCGAGGTATTCGCACCAGAGCCAACTGCTGT

Table 2. Primer sequences for qPCR

Gene	Forward primer (5'-3')	Reverse primer (5'-3')
LINC01123	CTCACTAAGTGGGCTGACCC	GGGATTCTGGCTTTTCCTGC
GAPDH	GGGAGCCAAAAGGGTCAT	GAGTCCTTCCACGATACCAA
miR-34c-5p	GGAGGCAGTGTAGTTAGCT	GTGCAGGGTCCGAGGT
miR-384	GTTTGGGGATTCCTAGAAATTG	GTGCAGGGTCCGAGGT
miR-876-5p	GTTGGGTGGATTTCTTTGTGAA	GTGCAGGGTCCGAGGT
miR-449b-5p	GTTTGGAGGCAGTGTATTGTTA	GTGCAGGGTCCGAGGT
miR-744-5p	TTGTTTGCGGGGCTAGGG	GTGCAGGGTCCGAGGT
U6	GCTTCGGCAGCACATATACTAAAAT	CGCTTCACGAATTTGCGTGTCAT

2.4. Cell transfection

Small interfering RNAs (siRNAs) targeting LINC01123, named si1-LINC01123, si2-LINC01123, and si3-LINC01123, were synthesized by General Biosystems (China). The sequences of the siRNAs and negative control (NC) are listed in **Table 3**. Overexpression or knockdown of miR-384 was performed using miR-384 mimics or inhibitors, respectively. The control plasmid (pcDNA3.1) and overexpression plasmids (pcDNA3.1-LINC01123) were synthesized by General Biosystems (Beijing, China). Lipofectamine 2000 reagent (Invitrogen, USA) was used to transfect siRNAs, miR mimics, miR inhibitors, and plasmids into cells according to the manufacturer's instructions.

Table 3. The sequences of siRNAs, miR mimics, and inhibitors used for transfection

Gene	Forward primer (5'-3')	Reverse primer (5'-3')
si1-LINC01123	CAGCAGAGAGAGAGAGGAATT	UUCCUCUCUCUCUCUGCUGTT
si2-LINC01123	CCACAGAGUAUGAAGGUCATT	UGACCUUCAUACUCUGUGGTT

Gene	Forward primer (5'-3')	Reverse primer (5'-3')
si3-LINC01123	CGGGAGAGGAGAAUGGAUUTT	AAUCCAUUCUCCUCUCCCGTT
NC	UUCUCCGAACGUGUCACGUTT	ACGUGACACGUUCGGAGAATT
miR-384 mimics	AUUCCUAGAAAUUGUUCAUA	UAUGAACAAUUUCUAGGAAU
NC mimics	UCACAACCUCCUAGAAAGAGUAGA	UCUACUCUUUCUAGGAGGUUGUGA
miR-384 inhibitor	UAUGAACAAUUUCUAGGAAU	
NC inhibitor	UCUACUCUUUCUAGGAGGUUGUGA	

2.5. Cell counting kit-8 (CCK-8) assay

The Cell Counting Kit-8 (CCK-8, DOJINDO, Japan) was used to evaluate cell proliferation. The cells were transfected with siRNAs, plasmids, mimics, or inhibitors, and incubated for 24 h. Cells were digested and resuspended in PBS for cell counting. Cells were seeded at a density of 2000 cells per well in 96-well plates. 10 μL CCK-8 reagent was added to each well at 24, 48, 72, and 96 h. Following incubation for 2 h, absorbance at 450 nm was measured using a microplate reader (BioTek Elx800, USA).

2.6. Cell migration assay

Cell migration was evaluated using a Transwell chamber insert (8 μm pore size, Corning, NY, USA). A density of 5×10^4 transfected cells suspended in 200 μL serum-free medium per well was seeded into the upper chambers of a 24-well polycarbonate membrane. Next, 800 μL of medium containing 10% FBS was added to the bottom chamber of the insert. After 24 h, the cells from the upper membrane to the bottom surface of the upper membrane were treated with methanol for 10 min and stained with 0.1% crystal violet for 10 min. Images were acquired under an inverted microscope (10X) and counted using ImageJ software.

2.7. Luciferase reporter assay

First, reporter plasmids were constructed. Fragments of wild-type LINC01123 and mutant LINC01123, containing miR-384 binding sites, were cloned into the pGL3-basic vector. The reporter plasmids were co-transfected into HEK-293T cells with miR-384 mimics or NC mimics using Lipofectamine 2000 reagent, according to the manufacturer's instructions. After 48 h of transfection, luciferase activity was detected using a luciferase assay kit (Promega, UAS), according to the manufacturer's protocols.

2.8. Statistical analysis

All statistical data were analyzed using the unpaired Student's *t*-test for comparisons between two groups. Figures were generated using GraphPad Prism software (version 8.0). All data are presented as the mean ± SEM. * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$ were considered to indicate statistically significant differences.

3. Results

3.1. LINC01123 is upregulated in lung cancer tissues and associated with progression of lung cancer

By analyzing GSE101929 and the TNMplot.com analysis platform, we found that the expression level of LINC01123 was upregulated in lung cancer tissues compared with normal tissues (**Figure 1A,B**).

Subsequently, we used the Kyoto Encyclopedia of Genes and Genomes to analyze the pathway and confirmed that LINC01123 participates in the progression of lung cancer (**Figure 1C**). The GEPIA dataset was used to analyze the differences in expression among different stages of the tumor, and the results suggested that there was a significant difference in the expression of LINC01123 among different stages of lung cancer (**Figure 1D**). Furthermore, the expression levels of LINC01123 were detected by qPCR in lung cancer cell lines, and the results showed that LINC01123 was highly expressed in A549 and H1975 cell lines (**Figure 1E**). These results indicate that LINC01123 is upregulated and associated with the progression of lung cancer.

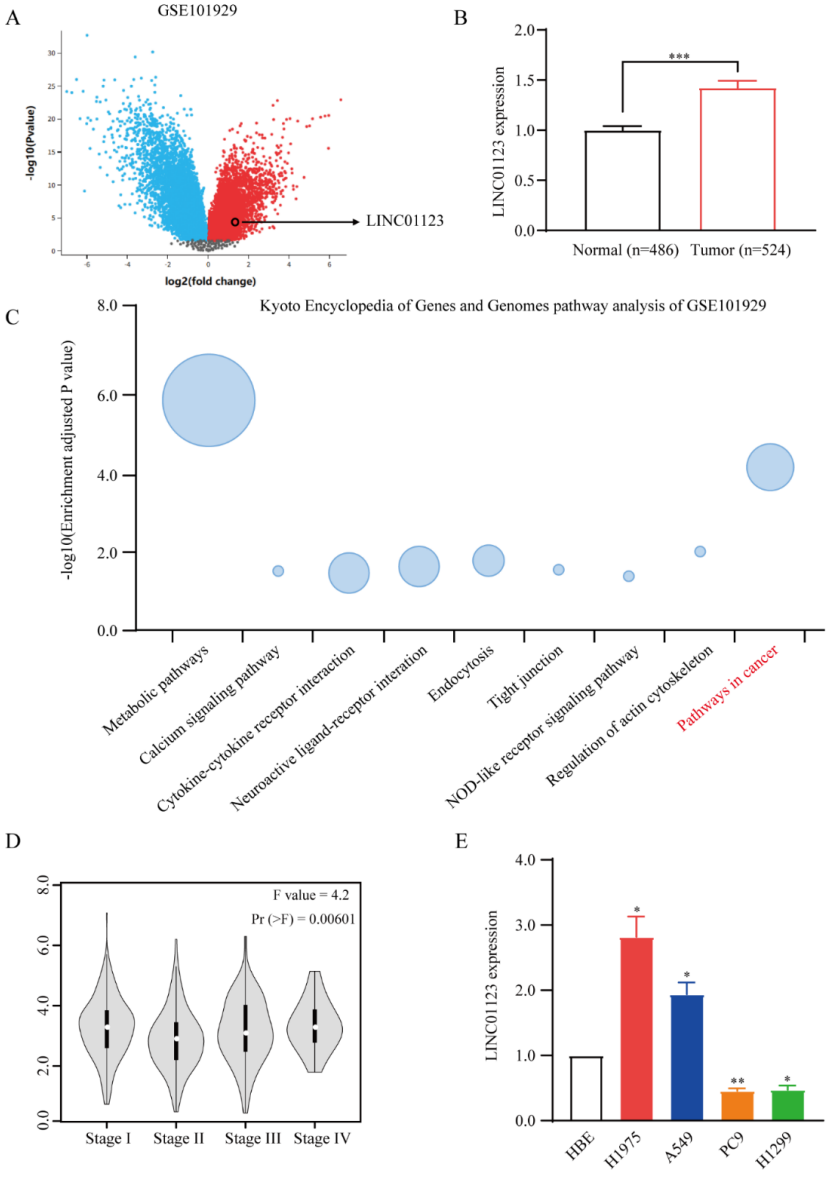

Figure 1. LINC01123 was upregulated in lung cancer tissues and cell lines and was involved in tumor progression. (A) The expression level of LINC01123 in lung cancer tissues was analyzed using the GEO dataset GSE101929, compared with normal tissues. (B) LINC01123 expression was analyzed between lung cancer tissues and normal tissues using the TNMplot website. (C) Kyoto Encyclopedia of Genes and Genomes pathway of GSE101929 was analyzed. (D) The relevance of LINC01123 expression to lung cancer pathologic stages was assessed based on information from the GEPIA database. (E) The expression level of LINC01123 in four lung cancer cell lines and the human bronchial epithelial cell HBE. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

3.2. LINC01123 promotes the proliferation and migration of lung cancer cells

To verify the biological roles of LINC01123 in lung cancer cells, we transfected small interfering RNA (siRNA) to knockdown the expression of LINC01123 in A549 and H1975 cells, and the efficiency was confirmed by qPCR (**Figure 2A, B**), and by transfection with pcDNA3.1-LINC01123 plasmid in PC9 cells to overexpress LINC01123 exogenously, and the efficiency was confirmed by qPCR (**Figure 2C**). CCK-8 and clone formation assays were performed to assess proliferation ability. The results of the CCK-8 assay showed that LINC01123 knockdown inhibited cell proliferation in A549 and H1975 cells (**Figure 2D, E**), whereas overexpression of LINC01123 had a contrasting effect in PC9 cells (**Figure 2F**). Cell migration was analyzed by performing the Transwell assay, and the results showed that the migratory ability was remarkably inhibited after knockdown of LINC01123 expression in A549 and H1975 cells (**Figure 2G, H**); conversely, overexpression of LINC01123 promoted migration in PC9 cells (**Figure 2I**). These results indicated that LINC01123 promotes lung cancer progression.

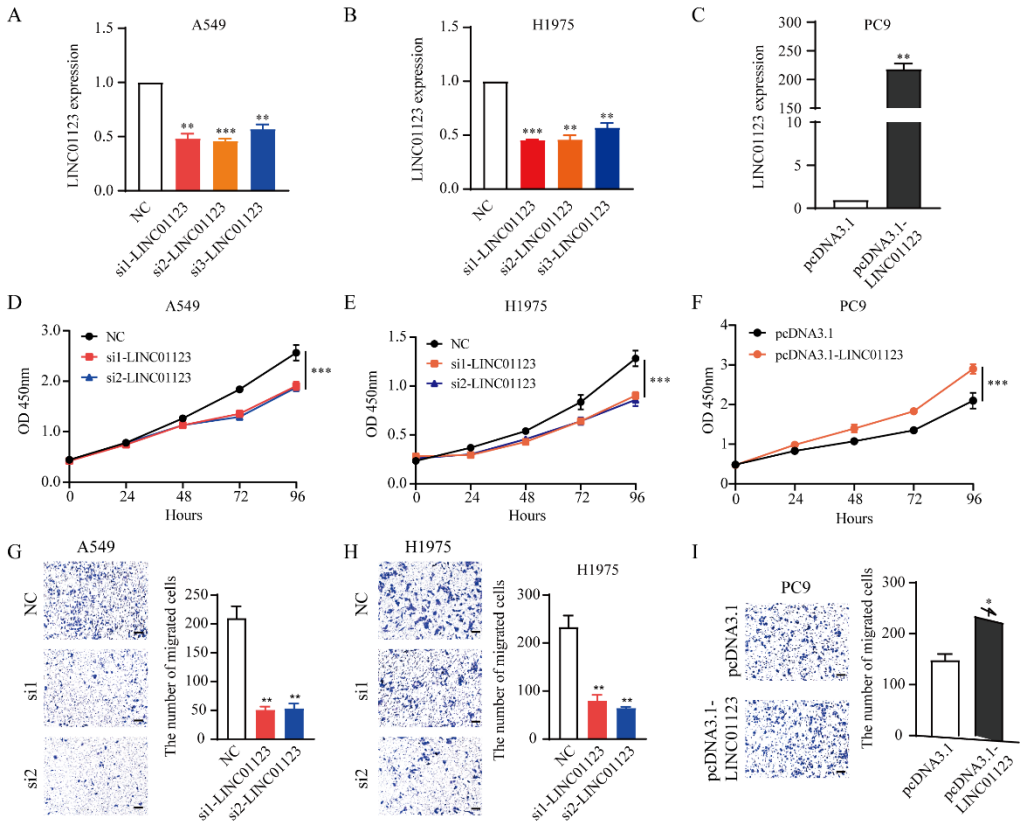

Figure 2. LINC01123 promoted lung cancer cell proliferation and migration *in vitro*. (A, B) The knockdown efficiency of LINC01123 was detected in A549 and H1975 cells by qPCR assay after transfection with si1-LINC01123, si2-LINC01123, and si3-LINC01123. (C) The overexpression efficiency of LINC01123 was detected in PC9 cells by qPCR assay after transfection with pcDNA3.1-LINC01123 plasmids. (D, E) CCK-8 assays were performed to assess the cell proliferation of A549 (D) and H1975 (E) cells after knocking down LINC01123. (F) For overexpression of LINC01123 in PC9 cells, the CCK-8 assay was used to assess the cell proliferation. (G, H) Transwell assays were performed to examine cell migration in A549 (G) and H1975 cells (H) transfected with LINC01123 siRNAs. (I) Transwell assays were performed to examine cell migration in PC9 cells transfected with pcDNA3.1-LINC01123 plasmids. Scale bar: 100 μm. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

3.3. LINC01123 can bind with miR-384 and regulates the expression of miR-384

To elucidate the mechanism underlying the role of LINC01123 in lung cancer carcinogenesis, we used StarBase, miRDB, and DIANA tools to predict candidate miRNAs that could bind to LINC01123, including miR-34c-5p, miR-384, miR-876-5p, miR-449b-5p, and miR-744-5p, which were downregulated in lung cancer. The expression of these miRNAs after knockdown of LINC01123 in H1975 and A549 cells was examined, and miR-34c-5p and miR-384 were found to be negatively correlated with LINC01123 (**Figure 3A, B**). We selected miR-384, which changed most significantly, for further research. The putative binding sites of miR-384 and LINC01123 were analyzed (**Figure 3C**). Based on the predicted results, we constructed LINC01123-WT and LINC01123-MUT plasmids for the luciferase reporter assay. The results showed that the luciferase activity of LINC01123-WT was significantly inhibited, but there was no obvious effect on the activity of LINC01123-MUT (**Figure 3D**). In conclusion, LINC01123 can directly bind to miR-384 and regulate its expression.

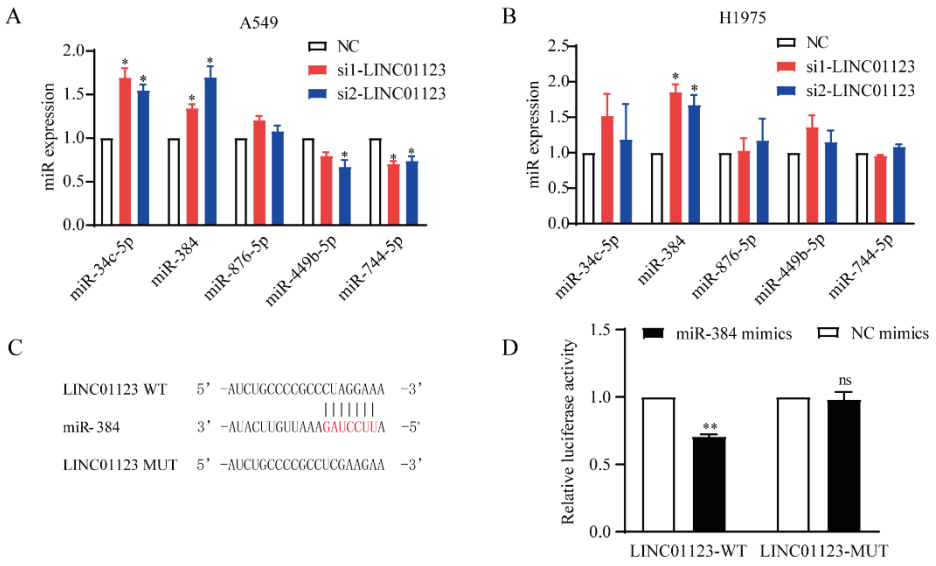

Figure 3. LINC01123 can bind to miR-384 and regulate the expression of miR-384. (A, B) The expression levels of five miRNAs were examined after LINC01123 knockdown in A549 (A) and H1975 cells (B) by qPCR assay. (C) The potential binding site between miR-384 and LINC01123 was predicted by StarBase online software. (D) A luciferase reporter assay was performed to assess the interaction between LINC01123 and miR-384. *: $p < 0.05$, **: $p < 0.01$.

3.4. Overexpression of miR-384 inhibits cell proliferation and migration of lung cancer

To determine the functional roles of miR-384 in lung cancer cells, we first detected the overexpression efficiency after transfecting miR-384 mimics into A549 cells (**Figure 4A**). CCK-8 and Transwell assays showed that cell proliferation and migration were inhibited after overexpression of miR-384 in A549 cells (**Figure 4B, C**). Taken together, these results indicate that miR-384 negatively regulates lung cancer cell proliferation and migration.

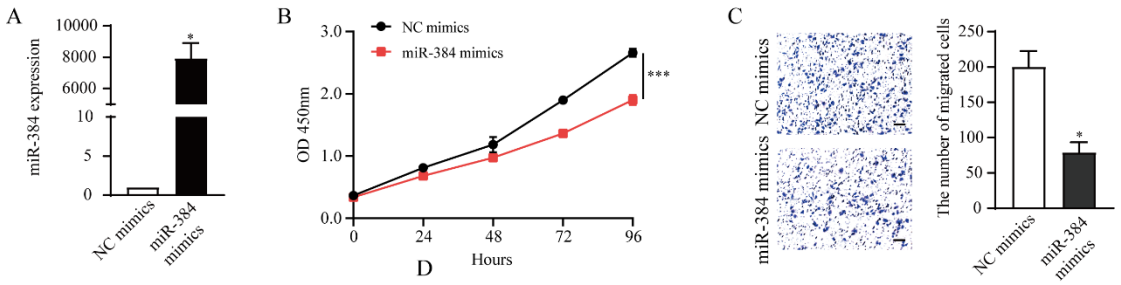

Figure 4. Overexpression of miR-384 inhibits cell proliferation and migration of lung cancer cells. (A) The overexpression efficiency of miR-384 when transfecting its mimics by qPCR assay. (B, C) The proliferation and migration when miR-384 is overexpressed in A549 cells by CCK-8 (B) and Transwell assays (C). Scale bar: 100 μm. *: $p < 0.05$, ***: $p < 0.001$.

3.5. Knockdown of miR-384 partially rescues the proliferation and migration of lung cancer cells, which are inhibited by LINC01123 silencing

To investigate whether miR-384 mediates the regulation of LINC01123 in lung cancer progression, we co-transfected si-LINC01123 and miR-384 inhibitor into A549 cells. CCK-8 assay showed that transfection with LINC01123 repressed cell proliferation, which was recovered by miR-384 depletion (**Figure 5A**). Similarly, cell migration was impaired by anti-miR-384, which was caused by LINC01123 knockdown in A549 cells (**Figure 5B**). These results indicated that LINC01123 promoted the progression of lung cancer by regulating the expression of miR-384.

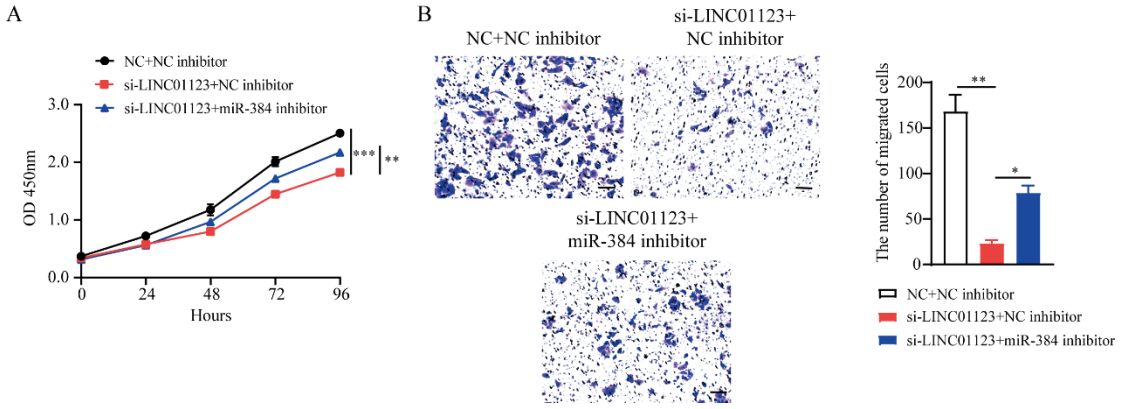

Figure 5. LINC01123 regulated the proliferation and migration of lung cancer cells via miR-384. (A) CCK-8 assay was used to evaluate cell proliferation. (B) Transwell assay was performed to assess cell migration. Scale bar: 100 μm. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

4. Discussion

Lung cancer is the most common malignancy and the leading cause of cancer-related death worldwide. Although great progress has been made in improving clinical treatment, the five-year survival rate of lung cancer patients is still low. Hence, there is an urgent need to identify new prognostic and therapeutic targets for clinical management. Increasing evidence has shown that lncRNAs can act as targets for the early diagnosis, therapy, and prognosis of lung cancer. In this study, we found that LINC01123 was upregulated in

lung cancer tissues and associated with tumor stage. Through a series of functional assays, the results showed that LINC01123 knockdown inhibited lung cancer cell proliferation and migration. Conversely, LINC01123 promoted proliferation and migration when LINC01123 was overexpressed in lung cancer cells. Based on these results, LINC01123 was found to play oncogenic roles in lung cancer cells.

MicroRNAs (miRNAs) are small noncoding RNA molecules encoded in the genome, approximately 22 nucleotides in length. miRNAs function by binding to the 3'-untranslated region (3'-UTR) of the target messenger RNA (mRNA) to negatively regulate gene expression, thus degrading the target mRNA and inhibiting gene translation [11]. In the progression of human cancer, some miRNAs have been identified as oncogenes or tumor suppressors, which may serve as biomarkers. For example, miR-539 inhibits breast cancer progression, and miR-205-5p contributes to lung cancer cell proliferation and migration [12,13]. MiR-384 has been reported to act as a suppressor in many tumors, such as colorectal cancer, renal cell carcinoma, osteosarcoma, and lung cancer [14,15]. In our study, we verified the functions of miR-384 in lung cancer cells and revealed the novel mechanism of the LINC01123/miR-384 regulatory pathway for the first time.

5. Conclusions

In general, our results confirmed the oncogenic role of LINC01123. Additionally, we revealed a novel signaling pathway of the LINC01123/miR-384 axis for the first time. Our findings indicate that LINC01123 may be a potential diagnostic and therapeutic target for patients with lung cancer.

Funding

Huai'an Science and Technology Bureau (HAB202349) and Huai'an Municipal Health Commission (Project No.: HAWJ 202129)

Disclosure statement

The authors declare no conflict of interest.

References

[1] Thai A, Solomon B, Sequist L, et al., 2021, Lung Cancer. Lancet, 398(10299): 535–554.

[2] Hirsch F, Scagliotti G, Mulshine J, et al., 2017, Lung Cancer: Current Therapies and New Targeted Treatments. Lancet, 389(10066): 299–311.

[3] Ning J, Ge T, Jiang M, et al., 2021, Early Diagnosis of Lung Cancer: Which Is the Optimal Choice? Aging (Albany NY), 13(4): 6214–6227.

[4] Nooreldeen R, Bach H, 2021, Current and Future Development in Lung Cancer Diagnosis. International Journal of Molecular Sciences, 22(16): 8661.

[5] Liu C, Xiang X, Han S, et al., 2022, Blood-Based Liquid Biopsy: Insights into Early Detection and Clinical Management of Lung Cancer. Cancer Letters, 524: 91–102.

[6] Djebali S, Davis C, Merkel A, et al., 2012, Landscape of Transcription in Human Cells. Nature, 489(7414): 101–108.

[7] Hangauer M, Vaughn I, McManus M, 2013, Pervasive Transcription of the Human Genome Produces Thousands of Previously Unidentified Long Intergenic Noncoding RNAs. PLoS Genetics, 9(6): e1003569.

[8] Kung J, Colognori D, Lee J, 2013, Long Noncoding RNAs: Past, Present, and Future. Genetics, 193(3): 651–669.

[9] Schmitz S, Grote P, Herrmann B, 2016, Mechanisms of Long Noncoding RNA Function in Development and Disease. Cellular and Molecular Life Sciences, 73(13): 2491–2509.

[10] Shigeyasu K, Toden S, Ozawa T, et al., 2020, The PVT1 lncRNA Is a Novel Epigenetic Enhancer of MYC, and a Promising Risk-Stratification Biomarker in Colorectal Cancer. Molecular Cancer, 19(1): 155.

[11] Lin S, Gregory R, 2015, MicroRNA Biogenesis Pathways in Cancer. Nature Reviews Cancer, 15(6): 321–333.

[12] Cai F, Chen L, Sun Y, et al., 2020, MiR-539 Inhibits the Malignant Behavior of Breast Cancer Cells by Targeting SP1. Biochemistry and Cell Biology, 98(3): 426–433.

[13] Zhao Y, Zhang J, Yang J, et al., 2022, MiR-205-5p Promotes Lung Cancer Progression and Is Valuable for the Diagnosis of Lung Cancer. Thoracic Cancer, 13(6): 832–843.

[14] Wang Y, Zhu H, Zhang Z, et al., 2018, MiR-384 Inhibits the Proliferation of Colorectal Cancer by Targeting AKT3. Cancer Cell International, 18: 124.

[15] Yan L, Wu K, Du F, et al., 2019, MiR-384 Suppressed Renal Cell Carcinoma Cell Proliferation and Migration Through Targeting RAB23. Journal of Cellular Biochemistry, 120(2): 1420–1426.