LINC00922 Accelerates the Proliferation, Migration and Invasion of Lung Cancer Via the miRNA-204/CXCR4 Axis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: The aim of this study was to clarify the potential function of LINC00922 in regulating the progression of lung cancer and its underling mechanism.

Material/Methods: Relative levels of LINC00922 in lung cancer tissues and cell lines was determined by quantitative polymerase chain reaction. Correlation between LINC00922 levels and pathological indexes of lung cancer patients was analyzed through the chi-square test. Subsequently, regulatory effects of LINC00922 on the proliferative, migratory, and invasive capacities of PC9 and A549 cells were evaluated. Western blot was conducted to determine the role of LINC00922 in mediating protein levels of CXCR4, E-cadherin, and vimentin. Through dual-luciferase reporter gene assay and functional experiments, the potential function of LINC00922/miRNA-204/CXCR4 regulatory loop in mediating the progression of lung cancer was explored.

Results: LINC00922 was highly expressed in lung cancer and correlated to the poor prognosis of lung cancer patients. Overexpression of LINC00922 accelerated PC9 and A549 cells to proliferate, migrate, and invade. CXCR4 was upregulated in lung cancer tissues and cells, which promoted lung cancer cells to migrate and invade. LINC00922 regulated the level of CXCR4 and directly bound to miRNA-204/CXCR4. LINC00922 mediated the cellular behaviors of lung cancer cells via targeting the miRNA-204/CXCR4 axis.

Conclusions: LINC00922 was upregulated in lung cancer, and accelerated lung cancer cells to proliferate, migrate, and invade via targeting the miRNA-204/CXCR4 axis.

MeSH Keywords: **Lung Neoplasms • Receptors, CXCR4 • RNA, Long Noncoding**

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Background

Lung cancer is a malignancy worldwide, which seriously threatens human health owing to its high morbidity and mortality [1]. With the development of medical technology, the treatment of lung cancer has made great strides. Nevertheless, the average survival rate for lung cancer patients is 20% and the 5-year survival rate is lower than 15% since most of lung cancer patients are in the middle or advanced stage at diagnosis [2,3]. Currently, individualized therapy based on target genes at the cellular level are being studied, posing a promising application to improve the outcomes of lung cancer patients [4,5]. Therefore, it is of significance to fully elucidate the molecular mechanism of lung cancer.

Long non-coding RNA (lncRNA) mainly exists in nucleus or cytoplasm with a length greater than 200 nucleotides, and does not have protein-encoding functions [6–8]. LncRNA has diverse functions in physiological activities [9–12]. Recent studies have found the crucial functions of non-coding RNA (ncRNA) in regulating the progression of various types of cancers, including lung cancer [13–16]. For example, GAS5 is downregulated in non-small cancer lung cancer (NSCLC) and associated with tumor size and stage [17]. High level of HOTAIR is closely correlated to the prognosis of NSCLC patients, which could mediate the invasion and migration of NSCLC [18]. Overexpression of ANRIL stimulates the metastasis of lung cancer cells, and is related to the poor prognosis of the disease [19]. There are abundant unexplored lncRNAs related to lung cancer. As a newly discovered one, the role of LINC00922 in lung cancer remains unclear.

In 2011, Pandolfi et al. [20] proposed the ceRNA (competing endogenous RNA) hypothesis. They suggested that mRNA, pseudogene transcript and lncRNA sharing the common MRE (miRNA response element) could mediate target gene expression through competitively bind to the same miRNA. The ceRNA hypothesis illustrated a novel regulatory network and provided a creative direction in investigating cellular function and molecular mechanism. Previous studies have already reported that several lncRNAs could bind to target miRNAs, thus regulating cellular behaviors of tumor cells [21–24]. For example, MALAT1 upregulates SLUG by absorbing miRNA-204, thus accelerating the progression of lung adenocarcinoma [25]. NEAT1 aggravates the malignant progression of NSCLC through sponging miR-377-3p to upregulate E2F2 [26].

In this study, expression pattern of LINC00922 in lung cancer was firstly examined. Moreover, the regulatory effects of LINC00922/miRNA-204/CXCR4 regulatory loop on mediating the progression of lung cancer were further explored. Our study aims to provide novel directions and therapeutic targets for lung cancer.

Material and Methods

Data collection

The expression profiles of lung cancer were downloaded from The Cancer Genome Atlas (TCGA). The dysregulated lncRNAs were obtained by edgeR package. Lung cancer tissues (n=52) and normal lung tissues (n=52) were surgically resected and immediately preserved in liquid nitrogen. Clinical data of 52 lung cancer patients were collected, including age, gender, tumor size, tumor node metastasis (TNM) stage, and the statue of lymph node metastasis. Lung cancer cells A549, PC9, and H460 were cultured in Roswell Park Memorial Institute 1640 (RPMI-1640) (HyClone, South Logan, UT, USA) containing 10% fetal bovine serum (FBS) (Gibco, Rockville, MD, USA) and 1% penicillin-streptomycin in a 37°C, 5% CO_2 incubator. Medium was replaced every 1 to 2 days. Cell passage was conducted until 80% of confluence using trypsin containing 0.05% SDS (sodium dodecyl sulfate) at a ratio of 1: 3. This study was approved by the Ethics Committee of the First Medical Center of Chinese PLA General Hospital. Signed written informed consents were obtained from all participants before the study.

Cell transfection

Cells were transfected with shRNA-LINC00922, vector-LINC00922, shRNA-CXCR4, vector-CXCR4, shRNA-NC, vector-NC, miRNA-204 mimic, miRNA-204 inhibitor, or miRNA-204-NC using Lipofectamine 2000 (Invitrogen, Carlsbad, CA, USA). Fresh medium was replaced at 6 hours. Transfected cells for 24 hours were harvested for the following experiments.

Quantitative real-time polymerase chain reaction (qRT-PCR)

Total RNA was extracted from cells or tissues using TRIzol reagent (Invitrogen, Carlsbad, CA, USA) and quantified using the Nanodrop Spectrophotometer (IMPLEN GmbH, Munich, Germany). The extracted RNA was subjected to reverse transcription to cDNA using the PrimeScript RT reagent Kit (TaKaRa, Otsu, Japan). Finally, complementary deoxyribose nucleic acid (cDNA) was amplified using the SYBR Primix Ex Taq II kit (TaKaRa, Otsu, Japan) on the 7500 Real-Time PCR System (Applied Biosystems, Foster City, CA, USA). Each experiment was repeated in triplicate.

Western blot

Proteins were extracted from cells or tissues and loaded for electrophoresis. After transferring on a polyvinylidene fluoride (PVDF) membrane (Millipore, Billerica, MA, USA), it was blocked in 5% skim milk for 2 hours. Subsequently, the membrane was incubated with primary antibodies at 4°C overnight

and secondary antibodies for 2 hours on the other day. Bands were exposed by electrochemiluminescence (ECL) and analyzed by Image Software (NIH, Bethesda, MD, USA).

Dual-luciferase reporter gene assay

LINC00922/CXCR4-Wt and LINC00922/CXCR4-Mut were constructed based on the predicted binding sequences to miRNA-204. Cells were co-transfected with LINC00922/CXCR4-Wt or LINC00922/CXCR4-Mut and miRNA-204-NC/miRNA-204 mimic for 48 hours. After cell lysis, relative luciferase activity was determined. β-galactosidase was used as the internal reference.

Cell Counting Kit-8 (CCK-8)

Cells were seeded in a 96-well plate at a density of 2×10^4/mL. At the appointed time points, 10 µL of Cell Counting Kit-8 (CCK-8) solution (Dojindo, Kumamoto, Japan) was applied per well. After incubation for 2 hours, the recorded absorbance at 450 nm using a microplate reader was used for plotting the viability curve.

Colony formation assay

Cells were seeded in the 6-well plate with 500 cells per well. Each group had 3 replicate wells. After 2-week incubation, cells were subjected to fixation in 4% paraformaldehyde and 0.1% violet crystal staining for 20 minutes. Finally, colonies were captured for counting under a microscope.

Transwell assay

Transfected cells were subjected to starvation in serum-free medium for 3 hours, and re-suspended in medium containing 1% FBS. 5. $X\times10^4$ cells were seeded in the upper side of Matrigel-coated Transwell chamber (8 µm, Millipore, Billerica, MA, USA). In the bottom side, 600 µL of medium containing 10% FBS was applied. After 48 hours of incubation, invasive cells in the bottom side were subjected to fixation in 70% ethanol at 4°C for 30 minutes, crystal violet staining for 20 minutes and cell counting using a microscope. Penetrating cells were counted in 5 randomly selected fields per sample. Transwell migration assay was conducted in the same procedures except for Matrigel pre-coating.

Statistical analyses

Statistical Product and Service Solutions (SPSS) 17.0 was used for statistical analysis. Data were represented as mean ±SD (standard deviation). The t-test was used for analyzing intergroup differences. Comparison between groups was done using one-way ANOVA test followed by post hoc test (least significant difference). Correlation between LINC00922 levels and
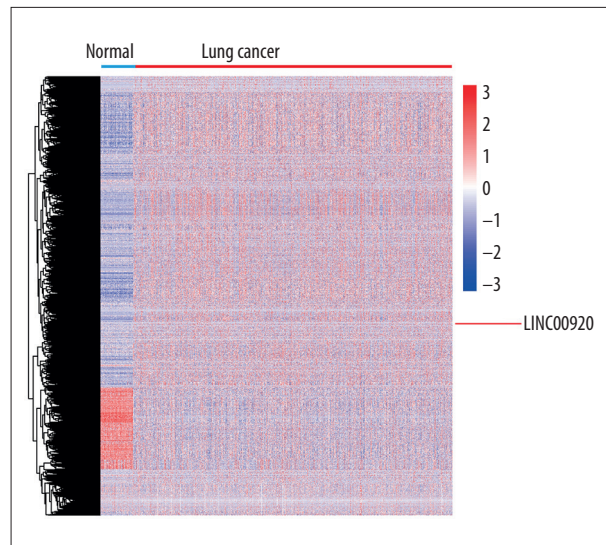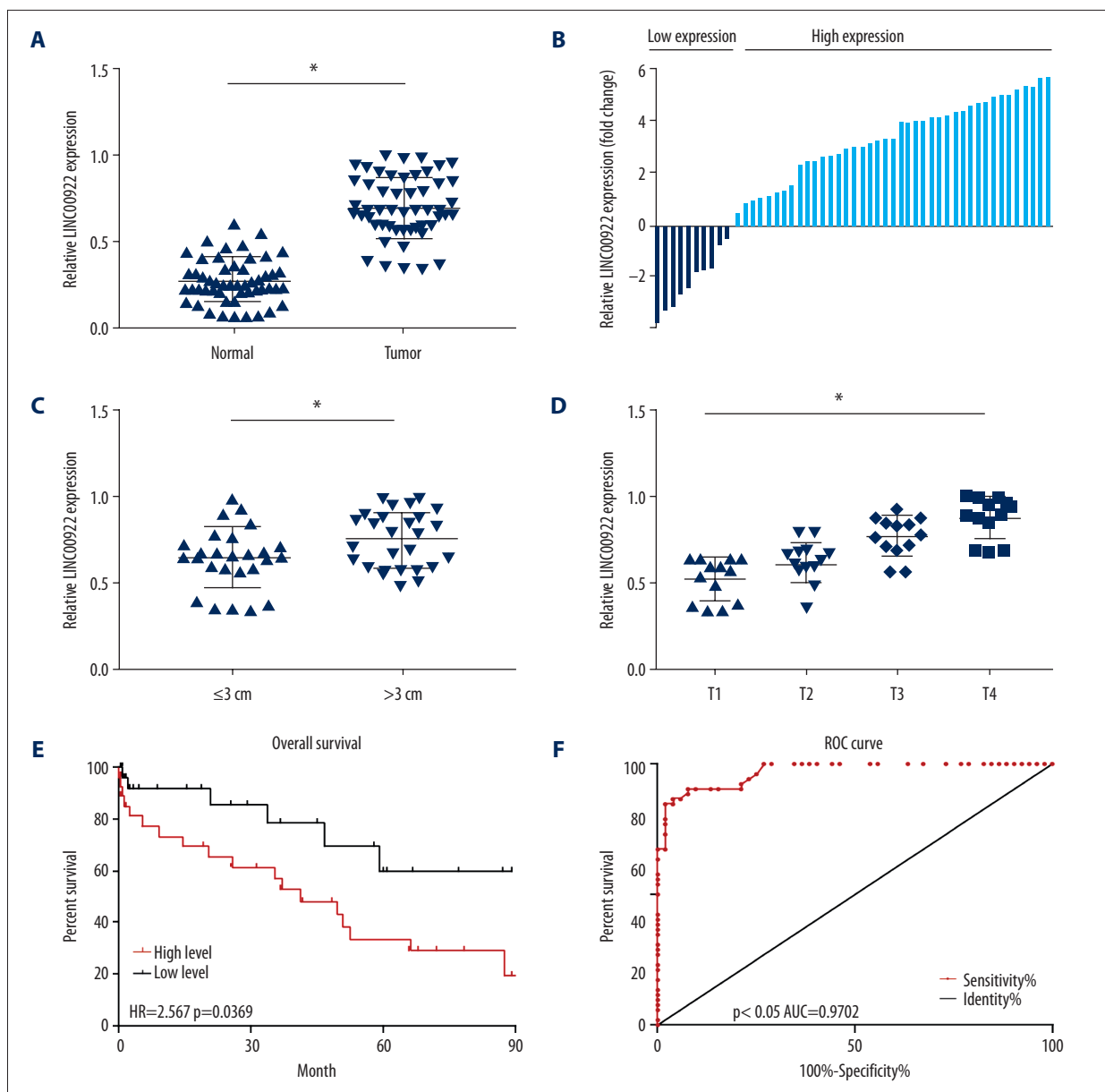

Figure 1. LINC00922 was upregulated in lung cancer in TCGA datasets.

pathological indexes of lung cancer patients was analyzed through the chi-square test. Kaplan-Meier and receiver operating characteristic (ROC) curves were introduced for survival analysis and diagnostic evaluation. $P<0.05$ indicated the significant difference.

Results

LINC00922 was upregulated in lung cancer and predicted a poor prognosis

LINC00922 level was higher in lung cancer tissues than normal tissues in the downloaded TCGA datasets analyzed by edgeR package (Figure 1). Expression pattern of LINC00922 in 52 cases of lung cancer tissues and normal lung tissues was determined by qRT-PCR. LING00922 was upregulated in lung cancer tissues as well (Figure 2A). Moreover, 52 lung cancer patients were divided into high-expression and low-expression group based on their LINC00922 level (Figure 2B). As Table 1 depicted, LINC00922 level was correlated to tumor size, TNM stage and lymph node metastasis of lung cancer. In particular, LINC00922 level was higher in lung cancer with tumor size >3 cm compared with those ≤3 cm (Figure 2C). Lung cancer patients in T2, T3, and T4 stage had higher level of LINC00922 relative to those in T1 stage (Figure 2D). Furthermore, follow-up data of enrolled patients were collected for survival analysis. Kaplan-Meier curve revealed a worse overall survival in lung cancer patients with high-level LINC00922 (Figure 2E). ROC curves illustrated the diagnostic potential of LINC00922 in lung cancer with a relatively high sensitivity (AUC=0.9702, Figure 2F). The aforementioned data illustrated that LINC00922 could be a prognostic marker for lung cancer.

Figure 2. LINC00922 was upregulated in lung cancer and predicted a poor prognosis. (**A**) Expression level of LINC00922 in 52 cases of lung cancer tissues and normal lung tissues determined by quantitative real-time polymerase chain reaction. (**B**) 52 lung cancer patients were divided into high-expression and low-expression group based on their LINC00922 level. (**C**) LINC00922 level in lung cancer with tumor size >3 cm and those ≤3 cm. (**D**) LINC00922 level in lung cancer patients in T1, T2, T3, and T4 stage. (**E**) Kaplan-Meier curve introduced based on LINC00922 level in lung cancer patients for survival analysis. (**F**) Receiver operating characteristic (ROC) curve introduced for the sensitivity and identity of LINC00922 in lung cancer diagnosis.

Overexpression of LINC00922 enhanced the proliferative ability of lung cancer cells

Compared with pulmonary epithelial cells line BEAS2B, LINC00922 was upregulated in lung cancer cell lines A549, PC9, and H460 (Figure 3A). Among the 3 lung cancer cell lines, PC9 and A549 cells expressed the highest and lowest level of LINC00922, respectively. Subsequently, transfection efficacy of

shRNA-LINC00922 in PC9 cells and vector-LINC00922 in A549 cells was verified by qRT-PCR (Figure 3B, 3C). CCK-8 and colony formation assay were conducted to evaluate the regulatory effect of LINC00922 on the proliferative capacity of lung cancer. Knockdown of LINC00922 in PC9 cells markedly decreased viability and clonality (Figure 3D, 3E). Conversely, overexpression of LINC00922 in A549 cells elevated viability and clonality (Figure 3F, 3G). These results revealed that LINC00922

Table 1. Correlation between LINC00922 level and pathological indexes of lung cancer patients (n=52).

Clinicopathologic features	Number of cases	LINC00922 expression		P-value
		Low (n=26)	High (n=26)	
Age (years)				
≤56	27	14	13	0.7814
>56	25	12	13	
Gender				
Male	21	11	10	0.7775
Female	31	13	16	
Tumor size				
≤3 cm	29	19	10	0.0120
>3 cm	23	7	16	
TNM stage				
I~II	25	17	8	0.0125
III~IV	27	9	18	
Lymph node metastasis				
Absent	24	16	8	0.0261
Present	28	10	18	

overexpression promoted the proliferative capacity of lung cancer cells.

Overexpression of LINC00922 accelerated lung cancer cells to invade and migrate

Transwell assay was conducted to evaluate invasive and migratory capacities of lung cancer cells influenced by LINC00922. Transfection of shRNA-LINC00922 attenuated invasive and migratory capacities of PC9 cells (Figure 4A). On the contrary, transfection of vector-LINC00922 in A549 cells enhanced migratory and invasive cell numbers (Figure 4B). It is well known that epithelial-mesenchymal transition (EMT) participates in the migration and invasion of tumor cells. Here, we determined expression levels of EMT-related genes in lung cancer cells influenced by LINC00922. Both mRNA and protein levels of E-cadherin were upregulated, while vimentin was downregulated in PC9 cells transfected with shRNA-LINC00922 (Figure 4C, 4D). Transfection of vector-LINC00922 downregulated E-cadherin and upregulated vimentin in A549 cells (Figure 4E, 4F). It is believed that LINC00922 overexpression enhanced migratory and invasive capacities of lung cancer, and accelerated EMT progression.

LINC00922 upregulated CXCR4 in lung cancer

Considering the carcinogenic role of LINC00922 in lung cancer, it is speculated that LINC00922 might exert its function by mediating CXCR4 level. As qRT-PCR data revealed, CXCR4 was

upregulated in lung cancer cells (Figure 5A). To further clarify the role of CXCR4 in the progression of lung cancer, shRNA-CXCR4 and vector-CXCR4 were constructed. Transfection of shRNA-CXCR4 downregulated mRNA and protein levels of CXCR4 in PC9 cells (Figure 5B, 5D, right panel). Meanwhile, transfection of vector-CXCR4 markedly upregulated its level in A549 cells (Figure 5C, 5D, left panel). Furthermore, it is demonstrated that knockdown of LINC00922 downregulated CXCR4 level, and LINC00922 overexpression upregulated CXCR4 level in lung cancer cells (Figure 5E). Therefore, LINC00922 positively regulated CXCR4 expression in lung cancer.

Overexpression of CXCR4 accelerated lung cancer cells to invade and migrate

Through Transwell assay, we found that transfection of shRNA-CXCR4 in PC9 cells decreased migratory and invasive cell numbers, and transfection of vector-CXCR4 in A549 cells obtained the opposite trends (Figure 6A, 6B). Furthermore, overexpression of CXCR4 upregulated E-cadherin and downregulated vimentin in lung cancer cells (Figure 6C). Knockdown of CXCR4 showed the opposite trends at protein levels of E-cadherin and vimentin (Figure 6D). CXCR4 was believed to be an oncogene in lung cancer cells.

MiRNA-204 bound to LINC00922 and CXCR4

MiRNA-204 was identified to bind to the 3'UTR sequences of LINC00922. Overexpression of miRNA-204 quenched
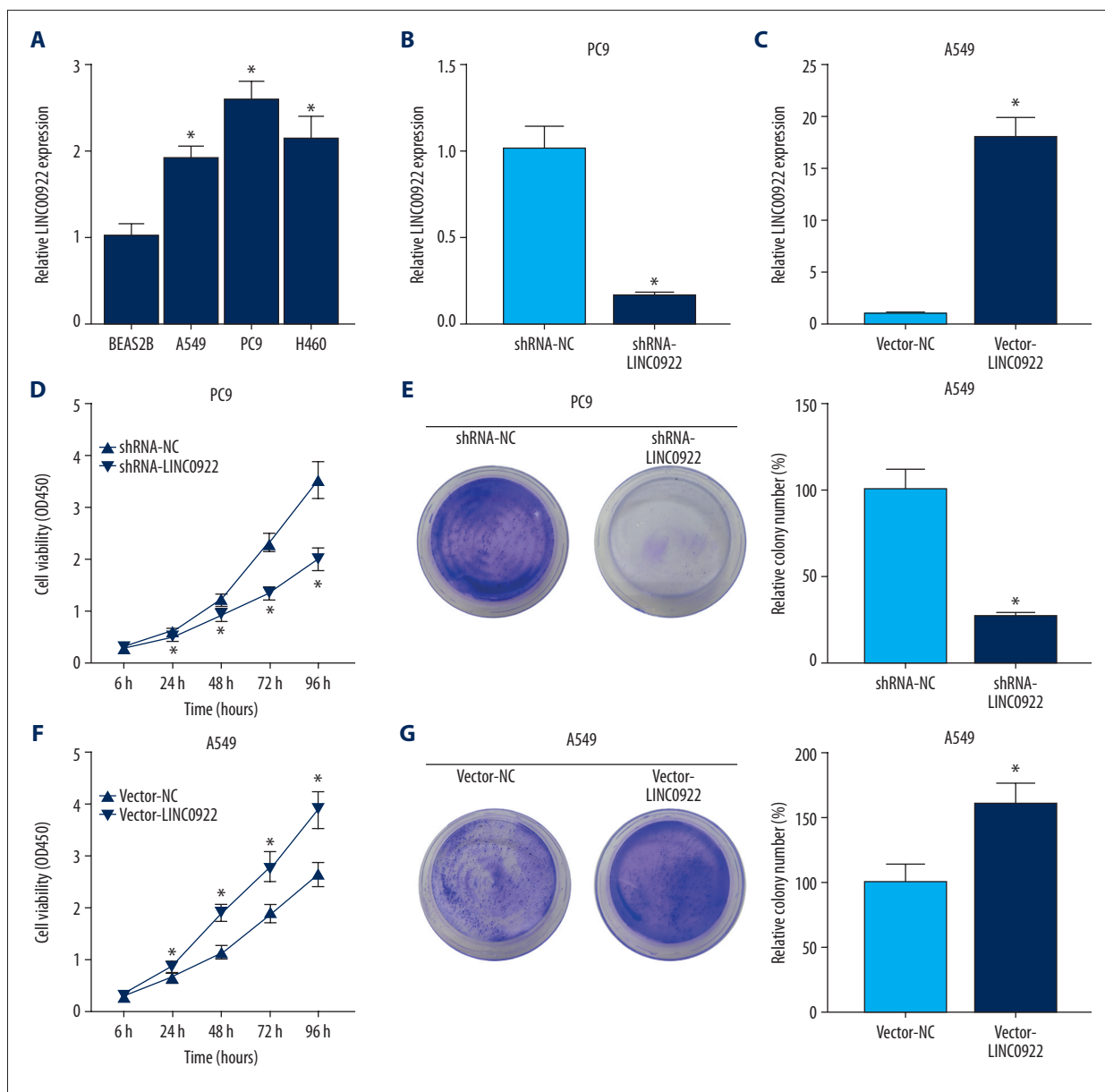
Figure 3. Overexpression of LINC00922 enhanced the proliferative ability of lung cancer cells. (**A**) Expression level of LINC00922 in pulmonary epithelial cells line BEAS2B and lung cancer cell lines A549, PC9, and H460 determined by quantitative real-time polymerase chain reaction (qRT-PCR). (**B**) Transfection efficacy of shRNA-LINC00922 in PC9 cells determined by qRT-PCR. (**C**) Transfection efficacy of vector-LINC00922 in A549 cells determined by qRT-PCR. (**D**) Cell Counting Kit-8 (CCK-8) assay revealed viability in PC9 cells transfected with shRNA-NC or shRNA-LINC00922 at 6, 24, 48, 72, and 96 hours. (**E**) Colony formation assay revealed the relative colony number in PC9 cells transfected with shRNA-NC or shRNA-LINC00922. (**F**) CCK-8 assay revealed viability in A549 cells transfected with vector-NC or vector-LINC00922 at 6, 24, 48, 72, and 96 hours. (**G**) Colony formation assay revealed the relative colony number in A549 cells transfected with vector-NC or vector-LINC00922.

the luciferase activity of LINC00922 Mut, indicating the binding between miRNA-204 and LINC00922 (Figure 7A). Similarly, miRNA-204 could bind to CXCR4 as dual-luciferase reporter gene assay confirmed (Figure 7B). After verifying the transfection efficacy of miRNA-204 mimic, transfection of miRNA-204 mimic remarkably downregulated CXCR4 level (Figure 7C, 7D).

MiRNA-204 reversed the promotive effects of LINC00922 on invasive and migratory capacities of lung cancer cells

LINC00922 could be a ceRNA to competitively bind to miRNA-204, thus mediating the cellular behaviors of lung cancer cells. Here, LINC00922 knockdown inhibited viability
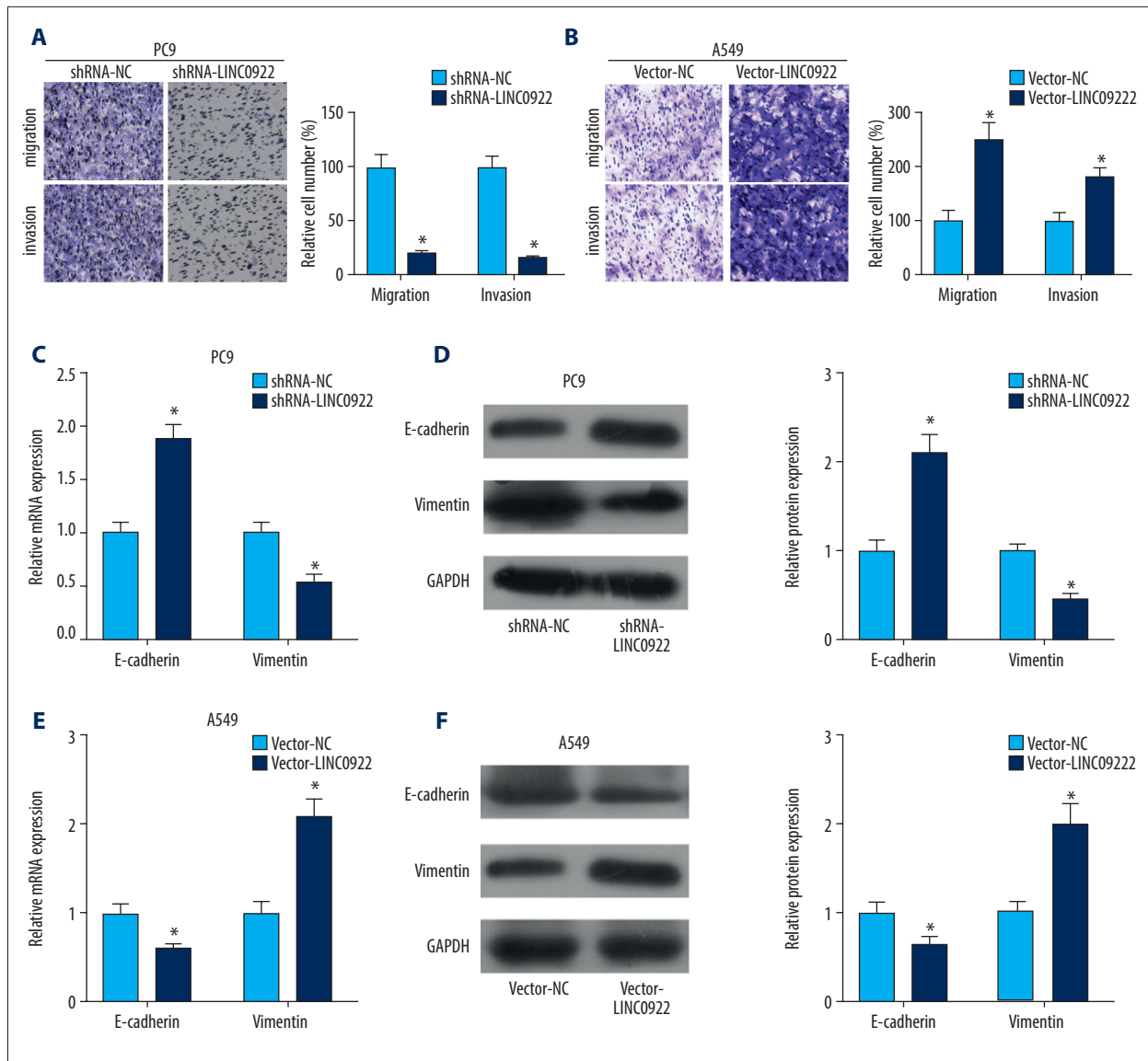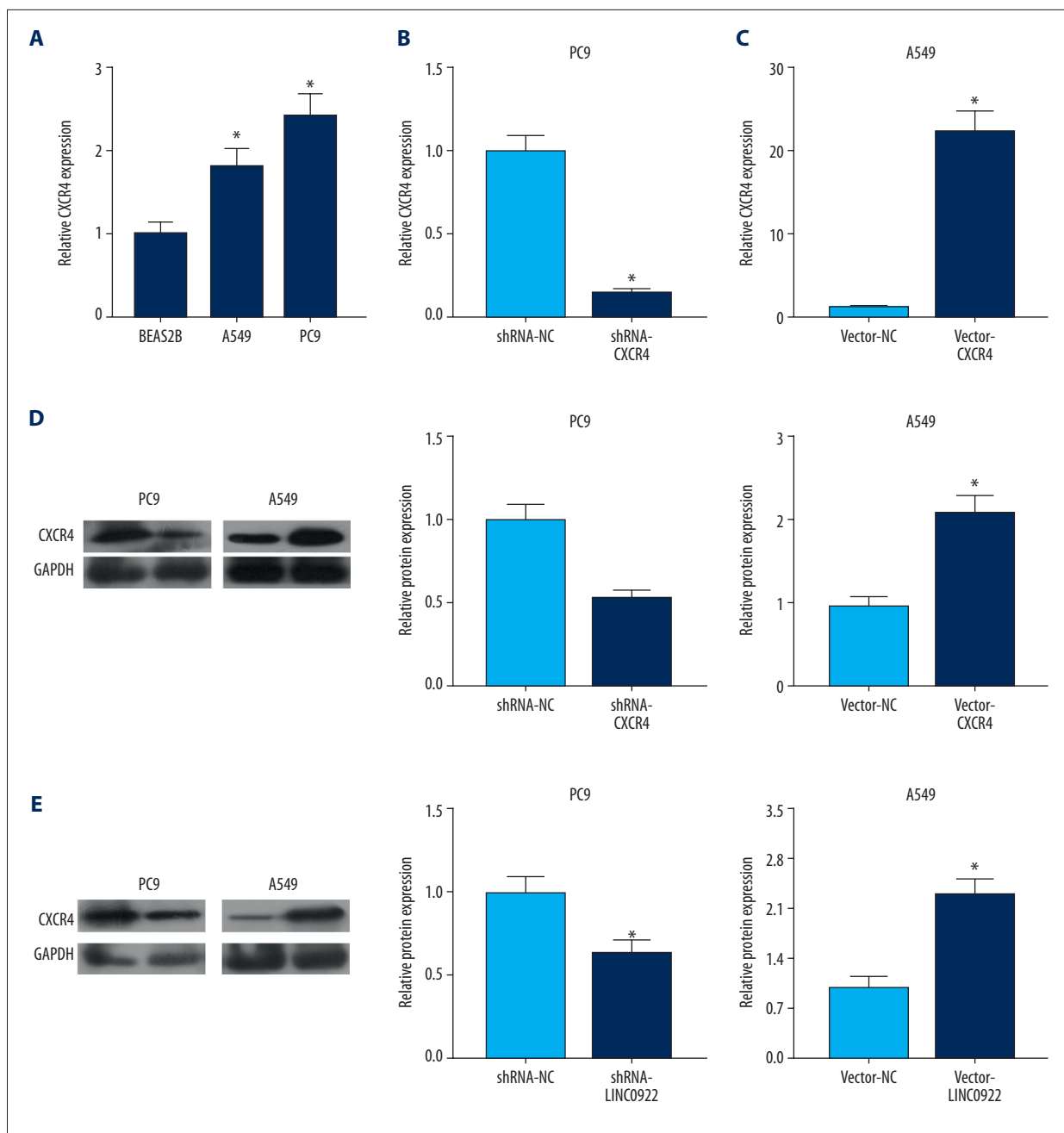
Figure 4. Overexpression of LINC00922 accelerated lung cancer cells to invade and migrate. (**A**) Transwell assay revealed the invasive and migratory cell number in PC9 cells transfected with shRNA-NC or shRNA-LINC00922. (**B**) Transwell assay revealed the invasive and migratory cell number in A549 cells transfected with vector-NC or vector-LINC00922. (**C**) Relative mRNA levels of E-cadherin and vimentin in PC9 cells transfected with shRNA-NC or shRNA-LINC00922. (**D**) Western blot analyses of E-cadherin and vimentin in PC9 cells transfected with shRNA-NC or shRNA-LINC00922. (**E**) Relative mRNA levels of E-cadherin and vimentin in A549 cells transfected with vector-NC or vector-LINC00922. (**F**) Western blot analyses of E-cadherin and vimentin in A549 cells transfected with vector-NC or vector-LINC00922.

of PC9 cells, which was partially reversed after miRNA-204 knockdown (Figure 8A). In A549 cells transfected with vector-LINC00922, the viability markedly increased, which was reversed by transfection of miRNA-204 mimic (Figure 8B). Identically, inhibited migratory and invasive capacities of PC9 cells with LINC00922 knockdown were partially reversed by miRNA-204 knockdown (Figure 8C). Similarly, the increased migration and invasion in A549 cells overexpressing LINC00922 were reversed by overexpression of miRNA-204 (Figure 8D).

Discussion

Lung cancer ranks first place in tumor death throughout the world, with a high mortality and mobility, and it is reported that approximately 2 2000 lung cancer cases are diagnosed yearly [27,28]. The prognosis of lung cancer is relatively poor, and the overall 5-year survival rate is only 16.6% according to previous studies [28]. Because most lung cancer patients are diagnosed at an advanced stage, and the metastatic *loci* and

Figure 5. (**A–E**) LINC00922 upregulated CXCR4 in lung cancer. (**A**) Transwell assay revealed the invasive and migratory cell number in PC9 cells transfected with shRNA-NC or shRNA-CXCR4. (**B**) Transwell assay revealed the invasive and migratory cell number in A549 cells transfected with vector-NC or vector-CXCR4. (**C**) Western blot analyses of E-cadherin and vimentin in PC9 cells transfected with shRNA-NC or shRNA-CXCR4. (**D**) Western blot analyses of E-cadherin and vimentin in A549 cells transfected with vector-NC or vector-CXCR4.

drug-resistance are easily developed at the early stage of treatment, the clinical outcomes of lung cancer remain poor [29]. Similar to other human malignant cancers, the imbalance of oncogenes and tumor-suppressor genes is found during the tumorigenesis, development, and progression of lung cancer [30].

RNA sequencing (RNA-seq) is a recently developed sequencing technology that recognizes unmapped genes, unrecognized non-coding RNAs, and splice variants [31–33]. RNA-seq provides a novel tool for clinical diagnosis and treatment of lung cancer [31–33]. Multiple miRNAs and lncRNAs have been proven to be closely related to the diagnosis and prognosis
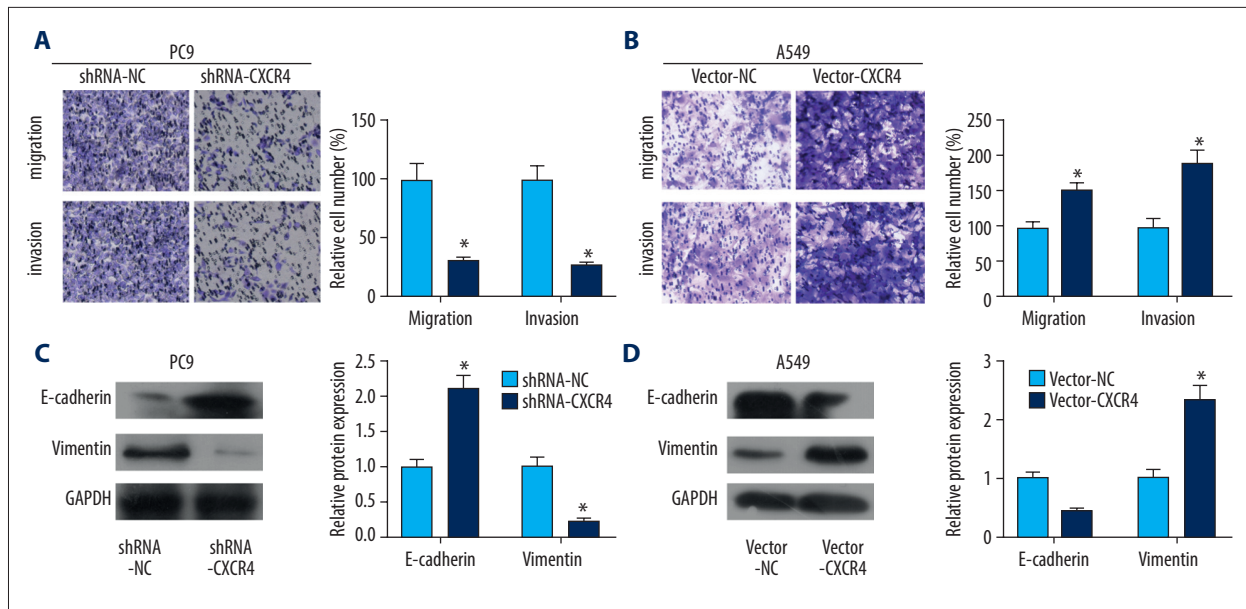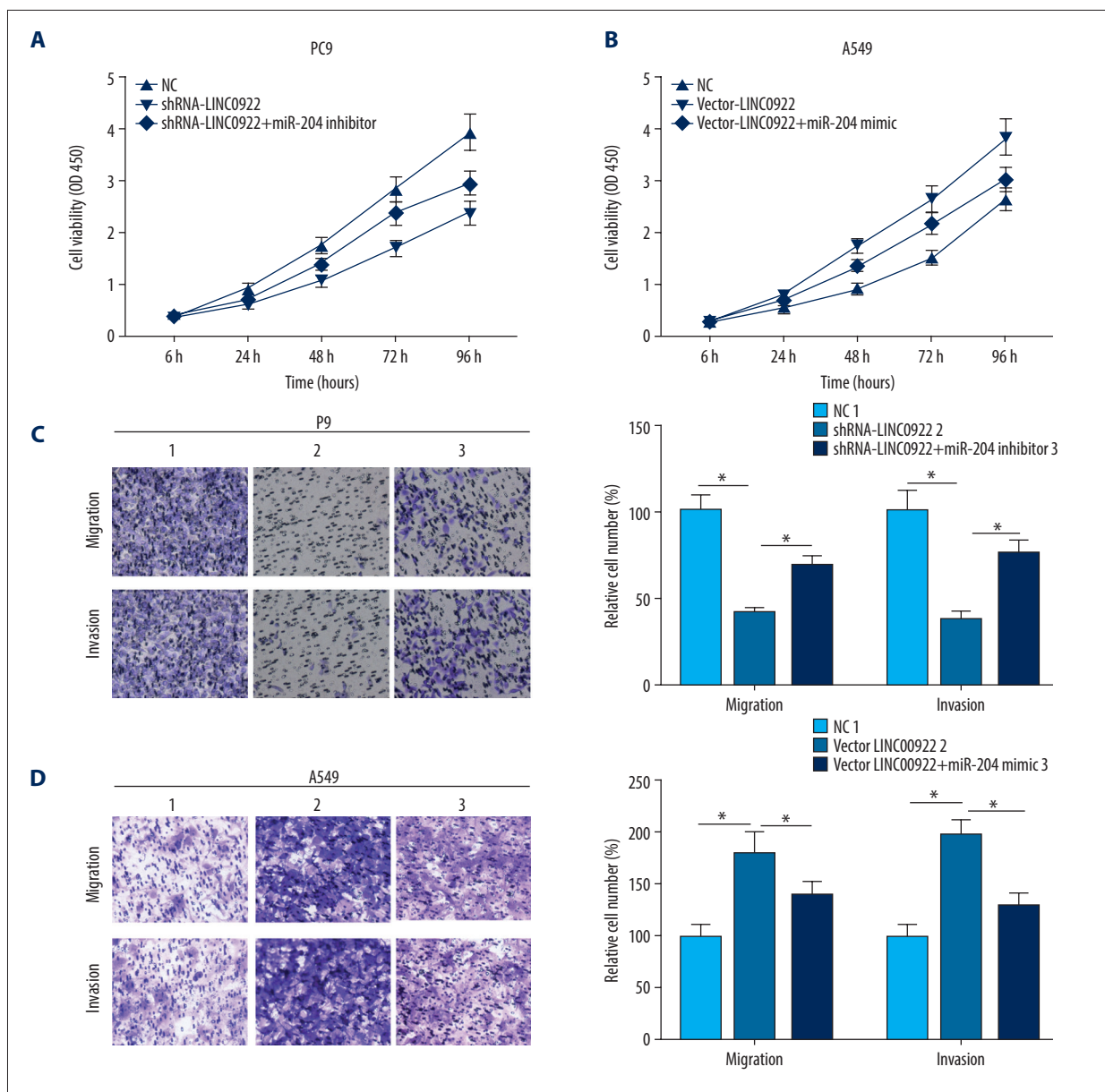
Figure 6. CXCR4 facilitated the invasive and migrated ability of lung cancer. (**A**) Knockdown of CXCR4 inhibited the invasive and migrated ability of PC9 cell line. (**B**) Overexpression of CXCR4 facilitated the invasive and migrated ability of A549 cell line. (**C, D**) The invasive and migrated markers were dysregulated while knocking down or overexpression of CXCR4.
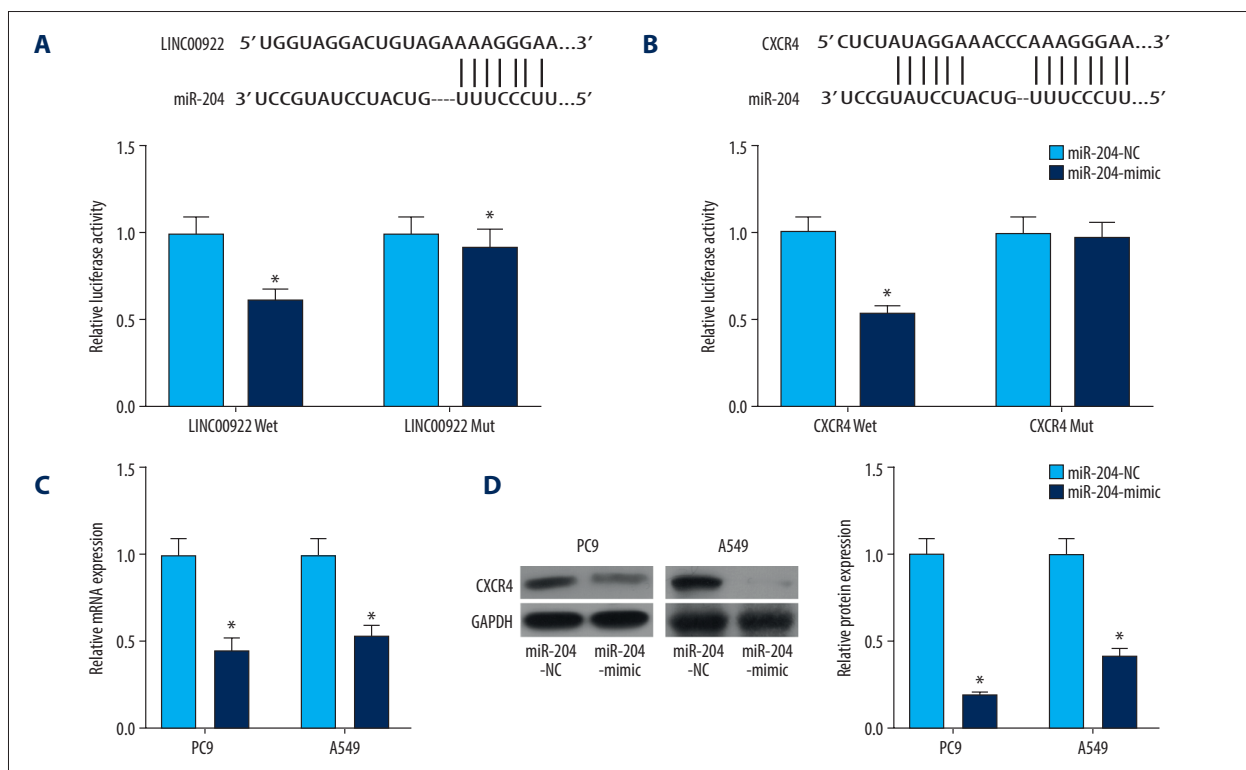
Figure 7. MiRNA-204 bound to LINC00922 and CXCR4. (**A**) Binding sequences of LINC00922 and miRNA-204 (**upper panel**). Relative luciferase activity in cells co-transfected with LINC00922-Wt/LINC00922-Mut and miRNA-204-NC/miRNA-204 mimic (**bottom panel**). (**B**) Binding sequences of CXCR4 and miRNA-204 (**upper panel**). Relative luciferase activity in cells co-transfected with CXCR4-Wt/CXCR4-Mut and miRNA-204-NC/miRNA-204 mimic (**bottom panel**). (**C**) Transfection efficacy of miRNA-204 mimic in PC9 and A549 cells determined by quantitative real-time polymerase chain reaction. (**D**) Western blot analysis of CXCR4 in PC9 and A549 cells transfected with miRNA-204-NC or miRNA-204 mimic.

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Figure 8. MiRNA-204 reversed the promotive effects of LINC00922 on invasive and migratory capacities of lung cancer cells. PC9 cells were transfected with NC, shRNA-LINC00922 or shRNA-LINC00922+miRNA-204 inhibitor, respectively. (**A**) Cell Counting Kit-8 (CCK-8) assay revealed viability in PC9 cells at 6, 24, 48, 72, and 96 hours. (**B**) CCK-8 assay revealed viability in A549 cells at 6, 24, 48, 72, and 96 hours. (**C**) Transwell assay revealed the invasive and migratory cell number in PC9 cells. A549 cells were transfected with NC, vector-LINC00922 or vector-LINC00922+miRNA-204 mimic, respectively. (**D**) Transwell assay revealed the invasive and migratory cell number in A549 cells.

of lung cancer [34,35]. With the contribution of next-generation sequencing, transcriptome sequencing of a large number of tumor samples and survival analysis, various tumor hallmarks have emerged [36]. In this study, LINC00922 was upregulated in lung cancer and closely related to poor prognosis. It is speculated that LINC00922 served as an ontogenetic role in lung cancer. Overexpression of LINC00922 accelerated lung cancer cells to proliferate, migrate, and invade.

Furthermore, LINC00922 had a certain impact on EMT, manifesting as upregulated E-cadherin and downregulated vimentin after overexpression of LINC00922.

CXCR4, a chemokine receptor, and its only agonist, CXCL12, have been reported to regulate the progression of solid tumors, including prostate cancer [37], breast cancer [38], colon cancer [39], and lung cancer [40,41]. CXCL16 has with many

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biological functions. Huang et al. [42] suggested that CXCL16 is highly expressed in various tumors such as breast cancer, pancreatic cancer, and prostatic cancer. Ke et al. [43] showed that CXCL16 is highly expressed in NSCLC patients, and also influences survival time. Moreover, silencing of CXCL16 not only suppresses proliferation of A549 and PC-9 cells, but also decreases their invasive ability [44]. In this study, CXCR4 was upregulated in lung cancer tissues. Its level was closely related to a poor prognosis of lung cancer patients. CXCR4 was upregulated in lung cancer cells as well. Overexpression of CXCR4 accelerated the proliferation and metastasis of lung cancer cells. EMT-related genes were found to be regulated by CXCR4 in lung cancer. Meanwhile, we further demonstrated that LINC00922 bound to CXCR4 and positively regulated its level in lung cancer cells. The specific mechanism of CXCR4 to promote lung cancer progression needs further investigations.

LncRNAs are reported to serve as ceRNAs to sponge miRNA, thus downregulating miRNA expressions [45]. For example, UCA1 upregulates the oncogene ERBB4 in lung cancer via binding to miR-193-3p [46]. LncRNA NORAD promotes cell proliferation and glycolysis in NSCLC by acting as a sponge for miR-136-5p [47]. To clarify whether LINC00922 served as a ceRNA to sponge a certain miRNA and further mediated CXCR4, dual-luciferase reporter gene assay was conducted

to verify the binding between miRNA-204 to LINC00922 and CXCR4. It showed that LINC00922 upregulated CXCR4 by competitively binding to miRNA-204. A previous study had already confirmed the inhibitory effect of miRNA-204 on the progression of NSCLC by mediating SIX1 level [48]. Here, our results illustrated that silencing of miRNA-204 could reverse the attenuated proliferative, migratory and invasive abilities in lung cancer cells with LINC00922 knockdown. Conversely, overexpression of miRNA-204 reversed the promotive effects of overexpressed LINC00922 on the cellular behaviors of lung cancer. The aforementioned results indicated that miRNA-204 could reverse the promotive role of LINC00922 in mediating the malignant behaviors of lung cancer cells, presenting as a tumor-suppressor gene.

Conclusions

LINC00922 was upregulated in lung cancer, and accelerated lung cancer cells to proliferate, migrate, and invade via the miRNA-204/CXCR4 axis as a ceRNA.

Conflict of interest

None.

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