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Regular paper

LINC00342 induces metastasis of lung adenocarcinoma by targeting miR-15b/*TPBG*

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In this study, the function and regulation of long non-coding RNA (lncRNA) *LINC00342* in lung adenocarcinoma were investigated. From The Cancer Genome Atlas (TCGA) datasets and Gene Expression Omnibus (GEO) datasets, *LINC00342* was found to be up-regulated in lung adenocarcinoma. The high expression of *LINC00342* was also validated in lung cancer cell lines. *LINC00342* induced invasion and epithelial–mesenchymal transition (EMT) process of A549 cells. By analyzing GEO datasets, *TPBG* was confirmed positively correlated to *LINC00342* and highly expressed in lung adenocarcinoma. In addition, *TPBG* induced invasion and EMT process of A549 cells. Through bioinformatics analysis and luciferase assay, miR-15b was validated as a direct target of both *LINC00342* and *TPBG*. Ectopic miR-15 expression repressed *LINC00342* and *TPBG*. Interestingly, *LINC00342* overexpression inhibited miR-15b and induced *TPBG*, whereas ectopic *TPBG* unchanged *LINC00342* and miR-15b levels. In conclusion, *LINC00342* promotes metastasis of lung adenocarcinoma through inducing *TPBG* targeted by miR-15b.

Key words: *LINC00342*, *TPBG*, miR-15b, metastasis, lung adenocarcinoma

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Abbreviations: EMT, Epithelial–mesenchymal transition; TPBG, Trophoblast glycoprotein; TCGA, The Cancer Genome Atlas; LUAD, lung adenocarcinoma; lncRNA, Long non-coding RNA; q-PCR, Quantitative real-time PCR; ceRNA, Competitive endogenous RNA; GEO, Gene Expression Omnibus; UTR, 3′-untranslational regions

INTRODUCTION

Lung cancer is one of the cancers with high mortality rate around the world. In all lung cancer types, lung adenocarcinoma accounts for more than 45% (Yang *et al.*, 2021). Although clinical treatments including surgery, radiotherapy and chemotherapy prolong the patient survival rate, the reoccurrence rate is still growing because of the metastasis (Xie *et al.*, 2021). Therefore, identification of potential bio-targets of metastasis is essential for overcoming the obstacle in lung adenocarcinoma.

In the last decade, long non-coding RNA (lncRNA) was identified to play important roles in cancer progression (Lopez-Jimenez & Andres-Leon, 2021). LncRNA contributes to multiple biological functions and processes including proliferation, apoptosis and metastasis (Tang *et al.*, 2021). Therefore, lncRNAs are a group of promising targets for cancer prevention. In this study, the function of lncRNA *LINC00342* in lung adenocarcinoma was investigated. Previous studies have shown that *LINC00342* is an oncogenic lncRNA which promotes metastasis and tumor growth in several cancers, including lung cancer (Chen *et al.*, 2019; Tang *et al.*, 2019; Miao *et al.*, 2020; Shen *et al.*, 2021). Here we clarified that *LINC00342* induced metastasis of lung adenocarcinoma through regulating *Trophoblast glycoprotein* (*TPBG*) and miR-15b.

TPBG is a transmembrane glycoprotein that is rarely expressed in normal human tissues (Hole & Stern, 1988; Southall *et al.*, 1990). Accumulating evidence indicated that *TPBG* is highly expressed in tumors such as bladder cancer, breast cancer and ovarian cancer (Southall *et al.*, 1990; Xylinas *et al.*, 2014; Stern & Harrop, 2017). In addition, high *TPBG* expression indicates a poor clinical outcome of gastric cancer (Gromova *et al.*, 2009). However, the function and underlying mechanism of *TPBG* in lung cancer are still elusive. In this study, we investigated the regulation of *TPGB* by lncRNA *LINC00342 via* miR-15b. The microRNA miR-15b was identified as a common target of both *LINC00342* and *TPBG*, which suggested a competitive endogenous RNA (ceRNA) regulation. Our findings confirmed *LINC00342*/miR-15b/*TPBG* regulatory axis, which provides a new direction for prevention of lung adenocarcinoma metastasis.

MATERIALS AND METHODS

Cell culture

A549, NCI-H1975, PG49 and NHLF fibroblasts were purchased from Cell Bank of the Chinese Academy of Sciences. A549 is a lung adenocarcinoma cell line derived from a 58-year-old Caucasian male. NCI-H1975 cells and PG49 cells were initially derived from non-small cell lung cancer tissue. All of these three cancer cell lines are epithelial cells. NHLF fibroblast is a normal primary cell from normal lung tissue. Cancer cells were cultured in RPMI-1640 medium (Gibco, USA) supplied with 10% fetal bovine serum (FBS, Gibco, USA) and cultivated in 5% CO_2, 37°C. NHLF was grown in Fibroblast Basal Medium (ATCC® PCS-201-030, USA) supplemented with Fibroblast Growth Kit-Low serum (ATCC® PCS-201-041, USA).

Vectors and RNAs

Overexpression of *LINC00342* and *TBPG* were realized through pcDNA3.1(+) vector cloning. Both inserted

sequences, synthesizing and vector construction, were performed by GenePharm (Shanghai, China). The sequence information of inserts was confirmed by Sanger sequencing. Verified overexpression vectors were named as pcD-L342 and pcD-TPBG, respectively. *LINC00342* and *TPBG* siRNAs and related scrambled siRNAs were designed and synthesized by Biomics (Nantong, China). MiR-15b mimics and negative control were ordered from Qiagen (Germany).

RNA extraction and quantitative real-time PCR (q-PCR)

After different treatments, total RNAs were extracted from cells by using High Pure RNA Isolation Kit (Roche, Switzerland). In each group, 100 ng RNA was used for reverse transcription to obtain cDNA. The q-PCR was performed in Light Cycler 480 system (Roche, Switzerland) and used SYBR Green PCR Master Mix (TaKaRa, Japan). *GAPDH* was served as an internal control for normalization. The relative quantitative comparison between the groups was evaluated using the $2^{-\Delta\Delta Ct}$ method.

Transfection

Cell transfection was performed according to the instructions provided by the manufacturers of transfection reagents. Briefly, for vector transfections, Lipofectamine 2000 (Invitrogen, USA) was used. The final amount of vector in each group is 2 μg in a 6-well plate. The ratio of Lipofectamine 2000 and vector is 1:1 (v/v). For siRNA and miRNA transfection, HiPerFect Transfection Reagent (Qiagen, Germany) was used. The final concentration of RNAs was 25 nM. The volume of transfection reagent used is 7 μl per well in a 6-well plate. The lipovector mixture was incubated for 5 min at room temperature. Then, added the mixture into cells dropwisely and cultivated for 48h.

Western blot

After different treatments, cells were lysed by RIPA buffer (50 mM Tris HCl, 150 mM NaCl, 1.0% (v/v) NP-40, 0.5% (w/v) Sodium Deoxycholate, 1.0 mM EDTA, 0.1% (w/v) SDS and 0.01% (w/v) sodium azide at a pH of 7.4). Total protein was quantified with BCA Kit (ThermoFisher, USA) according to the manufacturer's instructions. Total 30 μg protein was loaded and separated by SDS−PAGE and transferred onto PVDF membrane (Millipore, USA). Next, membranes were blocked with 5% skim milk dissolved in 1×TBST for 30 min at room temperature. The membranes were incubated with primary antibodies against TPBG (1:1000, Sigma−Aldrich) and Tubulin (1:5000, Sigma-Aldrich) at 4ºC overnight. The secondary antibody was incubated with membrane for 1h at room temperature. LI-COR Odyssey imaging system was employed to catch signals.

Transwell assay

After transfection and cultivation for 48h, cells were seeded into upper chamber (Millipore, USA) at the density of 5×10^4 cells/well, suspended in 200 μl medium without FBS in a 24-well plate. The lower chamber was filled with fresh medium containing 10% FBS. Cells were continuously cultivated for 48h. Cells in upper chamber were fixed by methanol for 30 min at room temperature. Then, carefully removed cells in the lower chamber and stained the chamber with 0.5% crystal violet for 15 min. The invasion rate was calculated by counting stained cell numbers.

Luciferase assay

The seed sequences of miR-15b in *LINC00342* and *TPBG* were cloned onto pGL3 control vector (Promega, USA). The whole procedure was performed by GenePharm (Shanghai, China). A549 cells were used for co-transfection of reporter vector and miRNA mimics. Cells were seeded into 24-well plate at the density of 2×10^4 cells/well and then co-transfected with 50 ng pGL3-L342 WT/MUT, 50 ng pGL3-TPBG WT/MUT vectors and 20 nM miR-15b mimics by HiPerfect Transfection Reagent (Qiagen, Germany). 20 ng Renilla vector was also co-transfected as normalization. The luciferase activity was measured according to the instructions of the Dual Luciferase Reporter assay after 48h cultivation.

Bioinformatic data analysis

The expression of *LINC00342* and *TPBG* in TCGA-LUAD was analyzed and obtained from GEPIA (http://gepia.cancer-pku.cn/index.html). The expression of *LINC00342* in GEO datasets were analyzed and the datasets were downloaded from GSE72762, GSE75342 and GSE89039. The correlation between *LINC00342* and *TPBG* was calculated and obtained from GEPIA (http://gepia.cancer-pku.cn/index.html), UALCAN (http://ualcan.path.uab.edu/index.html) and lnCAR (https://lncar.renlab.org/). The overall survival of lung adenocarcinoma patients correlated to *TPBG* expression was analyzed from GEPIA. *LINC00342* and *TPBG* targeted miRNAs were predicted through miRmap (https://mirmap.ezlab.org/). MiRNA expressions were analyzed from miR-TV (http://mirtv.ibms.sinica.edu.tw/).

Statistical analysis

All statistical analyses were performed using GraphPad Prism v8.0 (GraphPad Software, Inc.) software. All experiments were repeated in triplicate and the data are presented as the mean ±S.D. For associations between *LINC00342* expression and TPBG expression in LUAD Pearson's correlation analysis was used. A Student's *t*-test was used to compare two groups when the variance between groups was equal, and the Wilcoxon signed rank test was used in multi-group comparisons when the variance between groups was unequal. $P<0.05$, from a two-tailed test, was considered to indicate a statistically significant difference.

RESULTS

LINC00342 was up-regulated in lung adenocarcinoma

To investigate the expression *LINC00342* in lung adenocarcinoma, we analyzed gene expression data obtained from TCGA-LAUD datasets and three GEO datasets (GSE72762, GSE75342 and GSE89039) with clinical patient information. In the TCGA-LUAD results, *LINC00342* expression was up-regulated in tumor samples, whereas the difference was insignificant when compared to the normal samples (Fig. 1A). By analyzing GSE27262, GSE75324 and GSE89039, *LINC00342* was up-regulated significantly in tumor samples compared to normal group (Fig. 1B to 1D). To confirm the bioinformatics analysis results, we detected *LINC00342* expression in three lung adenocarcinoma cell lines including A549, NCI-H1975 and PG49. Indeed, compared to NHLF fibroblast, *LINC00342* was highly expressed in three cancer cell lines (Fig. 1E). Therefore,

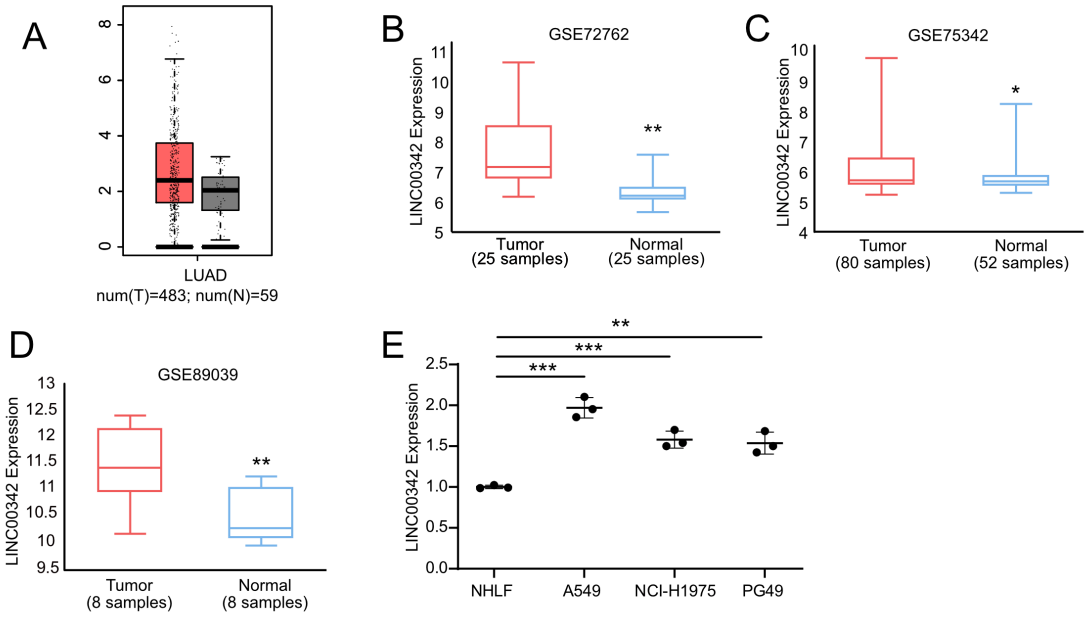

Figure 1. *LINC00342* was up-regulated in lung adenocarcinoma.
(**A**) Analysis of *LINC00342* expression in TCGA-LUAD datasets obtained from GEPIA. (**B**) to (**D**) Analysis of *LINC00342* expression in three GEO datasets including GSE72762, GSE75342 and GSE89039. (E) q-PCR analysis of *LINC00342* expression in three different lung cancer cell lines. *p<0.05, **p<0.01.

LINC00342 is a potential oncogenic lncRNA promoting lung adenocarcinoma progression.

LINC00342 induced metastasis of lung adenocarcinoma cells

Next, the function of *LINC00342* on metastasis was studied. Silencing or ectopic expression of

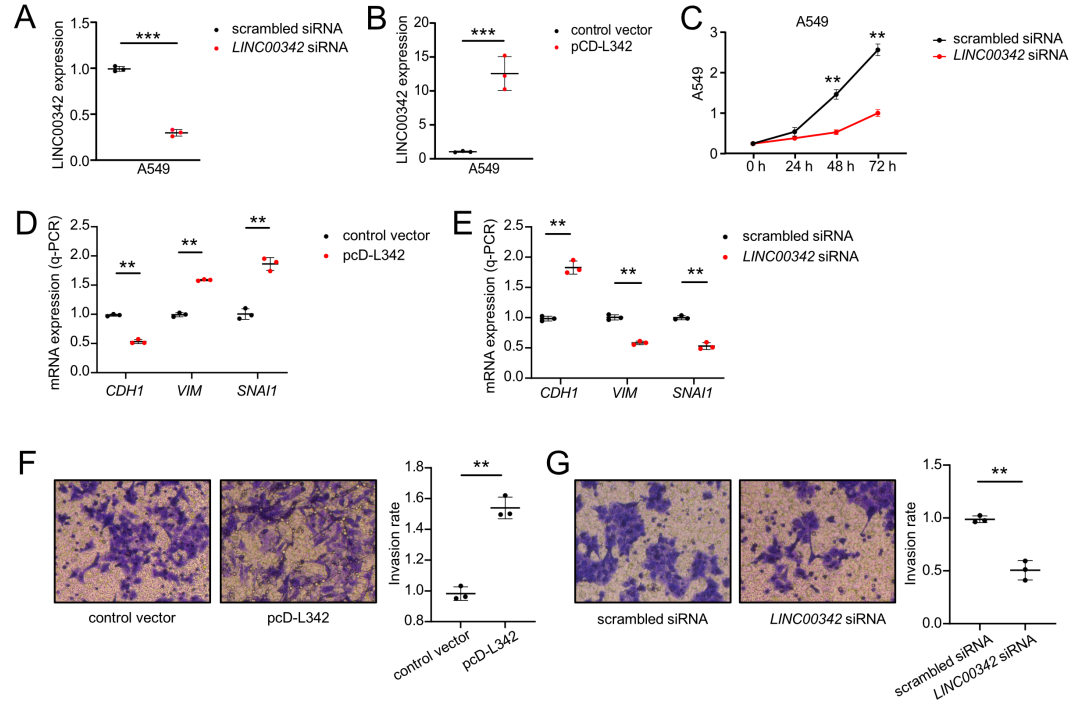

Figure 2. *LINC00342* induced metastasis of lung adenocarcinoma cells.
(**A**) q-PCR analysis of *LINC00342* expression after transfected with *LINC00342* siRNA and scrambled siRNA in A549 cells. (**B**) q-PCR analysis of *LINC00342* expression after transfected with overexpression vector pcD-L342 in A549 cells. (**C**) MTT analysis of proliferation rates of A549 cells at indicated time points after transfected with *LINC00342* siRNA. (**D**) q-PCR analysis of EMT markers after ectopically expressing *LINC00342* in A549 cells. (**E**) q-PCR analysis of EMT markers after silencing *LINC00342* in A549 cells. The invasion ability of A549 cells was evaluated by transwell assay after ectopically expressing (F) and silencing *LINC00342* (G). **p<0.01, ***p<0.001.

LINC00342 was achieved by specific *LINC00342* siRNA or overexpression vector (pcDNA-L342) in A549 cells, respectively (Fig. 2A and 2B). MTT analysis revealed that *LINC00342* silencing repressed proliferation ability of A549 cells (Fig. 2C). To further elucidate the function of LINC00342 in metastasis,

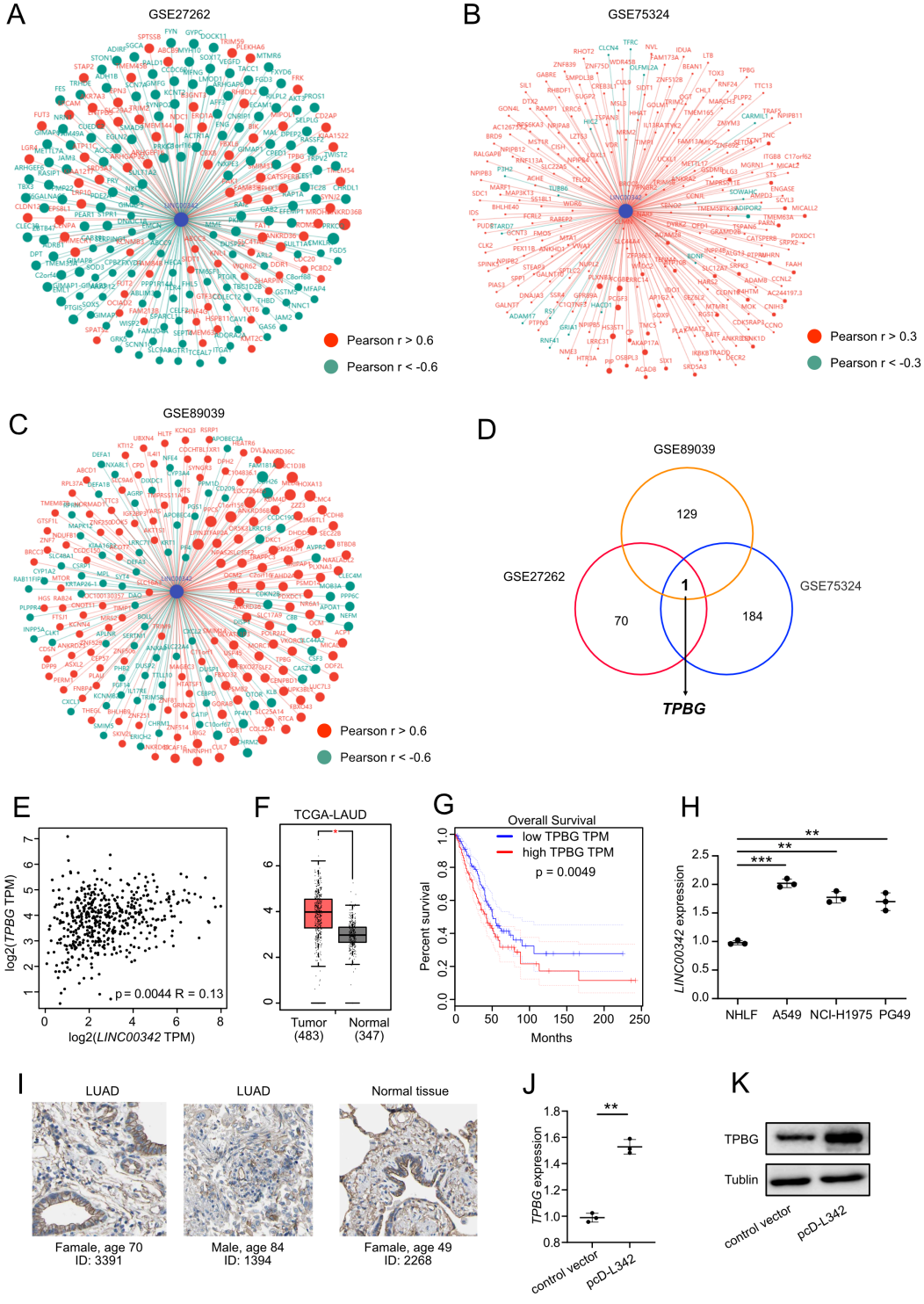

Figure 3. *TPBG* was positively related to *LINC00342* in lung adenocarcinoma.
Positive and negative corelated genes were analyzed from GSE27262, GSE75324 and GSE89039 and presented from (**A**) to (**C**). The positive corelated genes were marked with red while the negatives were marked with green. (**D**) Comparison of common up-regulated genes among GSE27262, GSE75324 and GSE89039. (**E**) The expression correlations between *TPBG* and *LINC00342* in TCGA-LUAD datasets was analyzed. (**F**) Analysis of TPBG expression in TCGA-LUAD datasets obtained from GEPIA. (**G**) The overall survival of high TPBG expression was analyzed in TCGA-LUAD datasets obtained from GEPIA. (**H**) q-PCR analysis of TPBG expression in three different lung cancer cell lines. (**I**) TPBG expression in tumor tissues and normal tissues were obtained from Human Protein Atlas. (**J**) q-PCR analysis of TPBG expression after ectopically expressing *LINC00342*. (K) Western blot analysis of TPBG expression after ectopically expressing *LINC00342*. **p*<0.05, ***p*<0.01, ****p*<0.001.

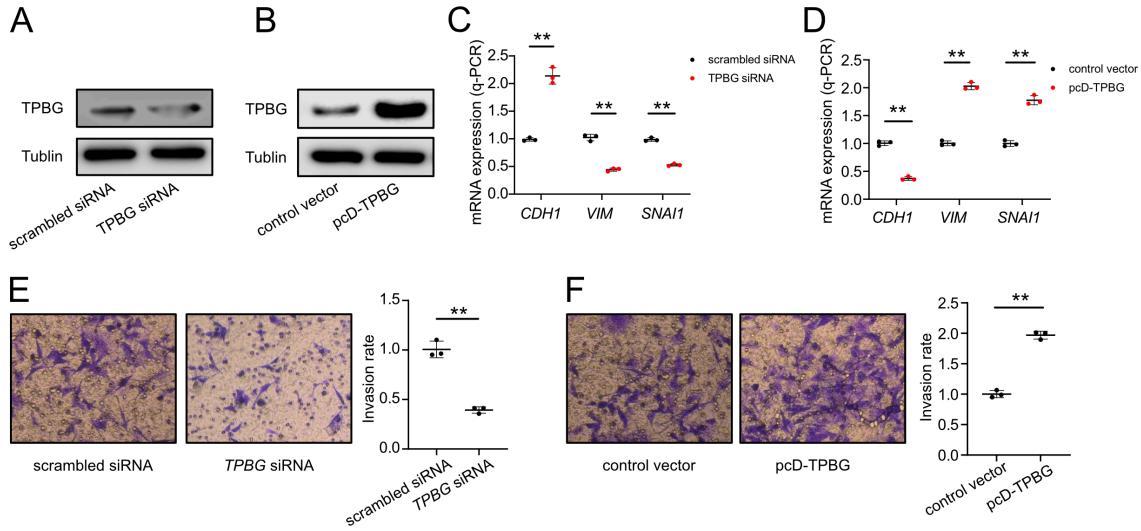

Figure 4. *TPBG* induced metastasis of lung adenocarcinoma cells.
(**A**) and (**B**) Western blot analysis of *TPBG* expression after transfected with TPBG siRNA and overexpression vector. (**C**) q-PCR analysis of EMT markers after silencing *TPBG* in A549 cells. (**D**) q-PCR analysis of EMT markers after ectopically expressing *TPBG* in A549 cells. The invasion ability of A549 cells was evaluated by transwell assay after silencing (**E**) and overexpressing *TPBG* (F). $^{**}p<0.01$.

we performed q-PCR analysis on EMT markers such as *CDH1*, *VIM* and *SNAI1*. Ectopic *LINC00342* repressed *CDH1* while *VIM* and *SNAI1* were induced by *LINC00342* (Fig. 2D). In addition, *LINC00342* silencing induced *CDH1,* whereas *VIM* and *SNAI1* were repressed (Fig. 2E). Above results indicated that *LINC00342* induces EMT process in lung adenocarcinoma cells. Furthermore, transwell assay showed that ectopic *LINC00342* induced A549 cell invasion ability (Fig. 2F). Conversely, silencing *LINC00342* repressed A549 cell invasion ability (Fig. 2G). In summary, *LINC00342* promotes lung adenocarcinoma metastasis *via* EMT process regulation.

TPBG was positively correlated to *LINC00342*

To investigate the landscape of *LINC00342* correlated gene expressions in lung adenocarcinoma, we analyzed GSE27262, GSE75324 and GSE89039 datasets to obtain positively and negatively correlated genes of *LINC00342*. The correlated genes with high-ranking scores were selected and presented from Fig. 3A to 3C. In total, 70 genes in GSE27262, 184 genes in GSE75324 and 129 genes in GSE89039 were positively correlated to *LINC00342* expression. Interestingly, by comparing the common correlated genes from three GEO datasets, only *TPBG* was obtained (Fig. 3D). Therefore, *TPBG* was the interesting gene correlated to *LINC00342* and investigated in the following studies. By analyzing the data of TCGA-LUAD datasets, *TPBG* also showed a positive correlation with *LINC00342* (Fig. 3E). In lung adenocarcinoma samples, *TPBG* was highly expressed compared to the normal samples (Fig. 3F). In addition, high *TPBG* expression indicated a lower overall survival rate in lung adenocarcinoma patients (Fig. 3G). Furthermore, we detected *TPBG* expression in three lung adenocarcinoma cell lines. Indeed, *TPBG* was highly expressed in lung adenocarcinoma cells compared to NHLF fibroblast (Fig. 3H). From the results of The Human Protein Atlas, *TPBG* also showed a high expression level in lung adenocarcinoma tissues of different patients (Fig. 3I). Interestingly, ectopic *LINC00342* further promoted *TPBG* expression in A549 cells, tested by q-PCR and western blot, respectively (Fig. 3J and 3K). Collectively, *TPBG* functions as an oncogene in lung adenocarcinoma, which is correlated to *LINC00342*.

TPBG induced metastasis of lung adenocarcinoma cell

Since we had identified that *TPBG* was highly expressed in lung adenocarcinoma and positively correlated to *LINC00342* expression, we then investigated the function of *TPBG* in metastasis of lung adenocarcinoma. *TPBG* was silenced by a specific siRNA (Fig. 4A) or ectopically expressed (Fig. 4B) by an overexpression vector (pcD-TPBG) in A549 cells. Q-PCR analysis indicated that *TPBG* silencing promoted *CDH1* expression, whereas *VIM* and *SNAI1* were repressed (Fig. 4C). Conversely, *TPBG* overexpression repressed *CDH1* while *VIM* and *SNAI1* were elevated (Fig. 4D). Furthermore, the invasion ability of A549 cell was inhibited by *TPBG* siRNA, whereas A549 cell invasion was enhanced by ectopic *TPBG* expression (Fig. 4E and 4F). Taken together, *TPBG* is an oncogene promoting metastasis of lung adenocarcinoma cell by EMT process regulation.

LINC00342 induced *TPBG* through targeting miR-15b

To study the potential regulation between *LINC00342* and *TPBG*, we analyzed the common target miRNAs of these two genes. A total 28 miRNAs targeting *LINC00342* and 41 miRNAs targeting *TPBG* were obtained. By comparing the two sets of miRNAs, 18 common miRNAs were obtained and presented in Fig. 5A. Next, we analyzed the expression of the 18 common miRNAs in TCGA-LUAD datasets. 8 miRNAs were highly expressed, and 6 miRNAs were down-regulated in lung adenocarcinoma compared to the normal group (Fig. 5B). Since both *LINC00342* and *TPBG* were up-regulated in lung adenocarcinoma, we focused on the down-regulated miRNAs in the following study. To confirm the results of bioinformatics analysis, we performed q-PCR analysis in three lung adenocarcinoma cell lines. Unexpectedly, only miR-15b, a well-studied tumor suppressor miRNA, was significantly down-regulated in all three cancer cell lines (Fig. 5C). From

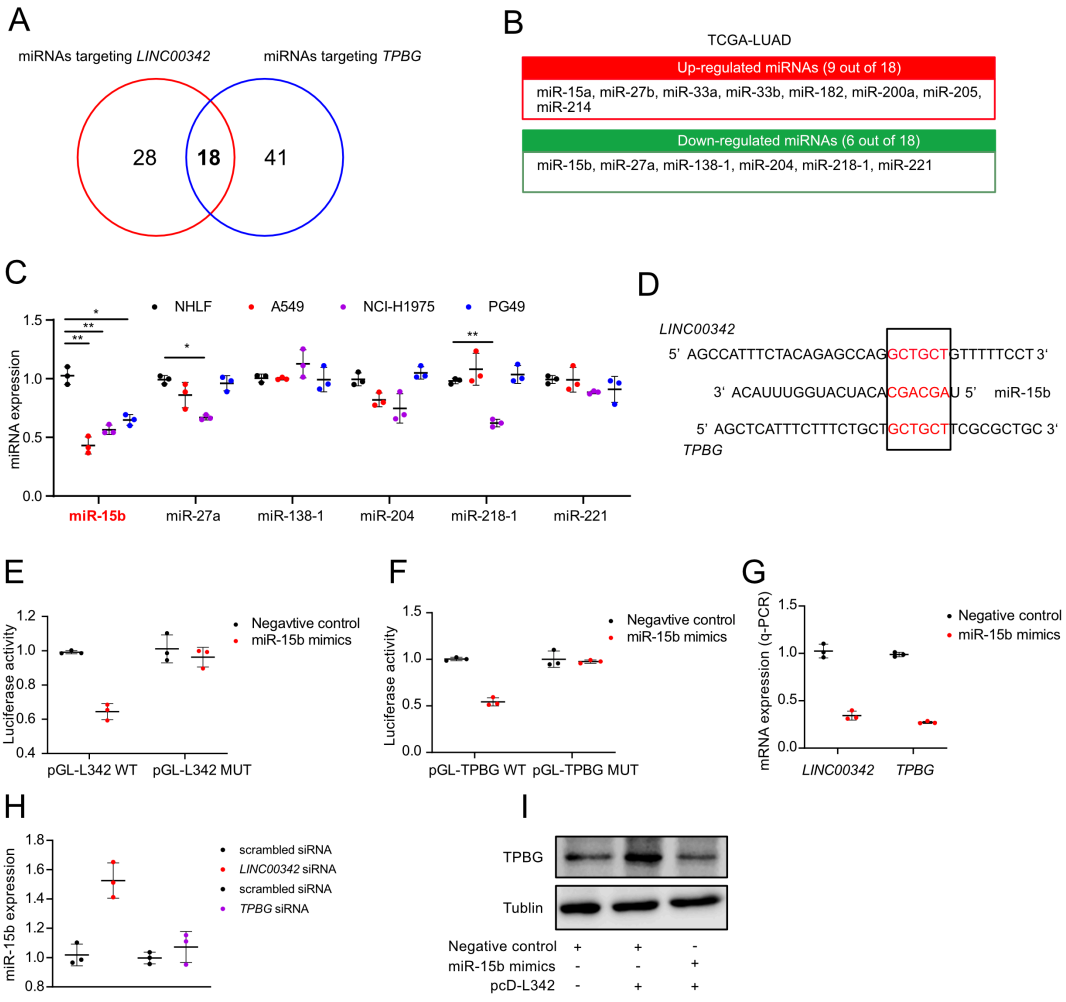

Figure 5. *LINC00342* induced *TPBG* through targeting miR-15b.
(**A**) Comparison of common miRNA targets of *LINC00342* and *TPBG*. Total 18 common miRNAs were obtained. (**B**) Obtained common miRNAs were analyzed based on TCGA-LUAD datasets. Up-regulated and down-regulated miRNAs in lung adenocarcinoma were presented. (**C**) q-PCR analysis of 6 down-regulated miRNAs expression in three lung cancer cell lines. (**D**) Both *LINC00342* and *TPBG* were predicted to be directly targeted by miR-15b at 3'UTR regions. The seed sequences were marked as red. Luciferase assay validated miR-15b directly targeted both *LINC00342* (**E**) and *TPBG* (**F**). (**G**) q-PCR analysis of *LINC00342* and *TPBG* expression after ectopically expressing miR-15b in A549 cells. (**H**) q-PCR analysis of miR-15b expression after silencing *LINC00342* and *TPBG* in A549 cells. (**I**) miR-15b partly reversed the effect of *LINC00342* on in ducing *TPBG* expression in A549 cells tested by western blot. *p<0.05, **p<0.01.

bio-informatic analysis, miR-15b was confirmed to target both *LINC00342* and *TPBG* through binding with seed-matching sequence in their 3'-untranslational (UTR) regions (Fig. 5D). The targets were validated by luciferase assay, which was represented by the significantly repressed luciferase activity of reporter vectors containing *LINC00342* and *TPBG* wild type seed sequences (Fig. 5E and 5F). Furthermore, ectopic miR-15b repressed *LINC00342* and *TPBG* expression in A549 cell, validated by q-PCR analysis (Fig. 5G). Interestingly, silencing *LINC00342* induced miR-15b expression, whereas silencing TPBG unchanged miR-15b level (Fig. 5H). Moreover, overexpression of *LINC00342* hardly promoted TPBG with ectopic miR-15b expression (Fig. 5I). Therefore, *LINC00342* induced *TPBG* through targeting miR-15b.

DISCUSSION

Lung cancer accounts for 10%-20% mortality rates among all cancer types around the world (Baldwin *et al.*, 2021). The low 5-year survival rate is mainly due to the high metastasis occurrence (Xie *et al.*, 2021). Lung adenocarcinoma is the most heterogenous and aggressive type compared to the other lung cancer types. In lung adenocarcinoma, non-small cell lung cancer has the highest proportion of patients (Tubio-Perez *et al.*, 2020). Recently, long non-coding RNA (lncRNA) was identified to play important roles in lung cancer progression (Chen *et al.*, 2021). Several lncRNAs were revealed aberrantly expressed in lung cancer. Here, we showed *LINC00342* was highly expressed in lung cancer. In previous studies, *LINC00342* was also identified to contribute to tumorigenesis. In NSCLC, *LINC00342* promotes metastasis and proliferation through targeting miR-203a-3p (Chen *et al.*, 2019). In addition, *LINC00342* is also a tumor biomarker of NSCLC, presented by high expression level in tissue and serum of NSCLC patients (Tang *et al.*, 2019). Tumor suppressor *p53* and *PTEN* are repressed by *LINC00342*, which results in promoted NSCLC proliferation (Wang *et al.*, 2016). In this study, we confirmed that *LINC00342* was highly expressed in lung adenocar-

cinoma patients. In line with the results of bioinformatics analysis, *LINC00342* was also up-regulated in three different lung cancer cell lines, indicating that *LINC00342* is an oncogenic lncRNA in lung adenocarcinoma. In functional analysis, ectopic *LINC00342* induced invasion ability of A549 cells. *LINC00342* promoted EMT process via repressing *CDH1*, whereas *VIM* and *SNAI1* expression were elevated.

Furthermore, we investigated *LINC00342* correlated genes in lung adenocarcinoma. Interestingly, *TPBG* was the only gene up-regulated together with *LINC00342* in all three GEO datasets. *TPBG* was first identified in human placental tissues. Normally, *TPBG* is rarely expressed in normal human tissues (Southall *et al.*, 1990). High TPBG expression was validated in various cancers including breast cancer, colorectal cancer and prostate cancer (Southall *et al.*, 1990; Xylinas *et al.*, 2014; Stern & Harrop, 2017). In our study, *TPBG* was confirmed to be up-regulated in lung adenocarcinoma. High *TPBG* expression was correlated to poor overall survivals. In addition, *TPBG* also promoted invasion of lung adenocarcinoma through the EMT process regulation.

Interestingly, both *LINC00342* and *TPBG* were directly targeted by miR-15b, which indicated a potential regulatory axis among these three molecules. In lncRNA regulation pattern, competitive endogenous RNA regulation is one of the most important and well-studied mechanisms. In previous studies, miR-15b was validated as a tumor suppressor miRNA in cancers. Nevertheless, miR-15b showed contradictive roles in lung cancer. In NSCLC, miR-15b is repressed by *MEG8*, which results in an elevated proliferation rate and promoted progression (Guo *et al.*, 2021). High serum miR-15b level is also a biomarker indicating a higher chemotherapy sensitivity (Shi *et al.*, 2020). Conversely, some studies also showed that miR-15b participates in tumor progression. The proliferation of NSCLC is promoted by miR-15b through targeting *TIMP2* (Wang *et al.*, 2017). In addition, miR-15b contributes to cisplatin resistance and metastasis in human lung adenocarcinoma via targeting *PEBP4* (Zhao *et al.*, 2015). In current research, we confirmed that miR-15b was repressed in lung adenocarcinoma patients and in three different lung cancer cell lines. Furthermore, miR-15b was validated as a direct target of both *LINC00342* and *TPBG*. Notably, *LINC00342* down-regulated miR-15b through RNA-RNA sponging. However, *TPBG* lacks the ability to repress miR-15b. Above results imply that miR-15b plays tumor suppressor roles. *LINC00342* induces *TPBG via* targeting miR-15b in lung adenocarcinoma.

In conclusion, *LINC00342* and *TPBG* are highly expressed in lung adenocarcinoma. *LINC00342* and *TPBG* induce metastasis of lung adenocarcinoma *via* regulating EMT process. MiR-15b serves as a tumor suppressor by targeting *LINC00342* and *TPBG*. *LINC00342* induces *TPBG via* targeting miR-15b in lung adenocarcinoma.

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Conflicts of Interests

Authors declare that there is no conflict of interest in this study.

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