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Research paper

Knockdown of *HNRNPA1* inhibits lung adenocarcinoma cell proliferation through cell cycle arrest at G0/G1 phase

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ABSTRACT

Heterogeneous nuclear ribonucleoprotein A1 (HNRNPA1), a member of heterogeneous nuclear ribonucleoprotein family in actively growing mammalian cells, is involved in a variety of RNA-related processes. HNRNPA1 can enhance the degradation of inhibitory subunit of nuclear factor κ B alpha (IκBα) and lengthen the telomeres. Recently, it is reported that HNRNPA1 is aberrantly expressed in varied tumors. In this study we found HNRNPA1 protein overexpressed in lung cancer tissues. To explore the exact role of HNRNPA1 in lung cancers, we carried out a loss of function analysis of HNRNPA1 in A549 lung cancer cells by RNA interference (RNAi). The results demonstrated that knockdown of *HNRNPA1* inhibited cell viability and colony formation of lung cancer cells and arrested cell cycle in G0/G1 phase. Our study suggested that *HNRNPA1* might play an important role in lung adenocarcinoma cells and provided a foundation for further study into the potential of *HNRNPA1* for lung cancer therapy.

1. Introduction

Lung cancer is the leading cause of cancer related death among men worldwide and is the second among women, with a 5-years survival rate is only 18% (DeSantis et al., 2014). Lung cancers are classified as small cell lung cancer (13%) and non-small cell lung cancer (NSCLC) (87%) according to the purposes of treatment (Siegel et al., 2014). Surgical resection remains the mainstay of treatment for early-stage NSCLC. Unfortunately, the majority of lung cancers are diagnosed at an advanced stage. For advanced NSCLC, platinum-based regimen is presently the standard first-line chemotherapy (Zarogoulidis et al., 2013). However, the response rate to chemotherapy was less than 30%. What's worse, many patients suffered serious side effect after chemotherapy. Target therapy, especially the use of tyrosine kinase inhibitors (TKIs) has improved the outcome of those patients. But, TKIs just benefit for the patients with EGFR mutation (Antonicelli et al., 2013), ranging from ~15% in Caucasians to ~50% in East Asians (Pao & Girard, 2011), and 95% of them are adenocarcinomas (Yamamoto et al., 2009). Thus, to further explore valuable diagnostic and novel therapeutic targets is in urgent need.

Heterogeneous nuclear ribonucleoproteinA1 (HNRNPA1) is one of the most abundant nuclear proteins in actively growing mammalian cells (Izaurralde et al., 1997). HNRNPA1 may interact simultaneously with telomerase RNA in vitro and maintain the length of telomeres (Fiset & Chabot, 2001; LaBranche et al., 1998). HNRNPA1 also plays an important role in enhancing the degradation of inhibitory subunit of nuclear factor κ B alpha (IκBα) degradation, resulting in the activation of nuclear factor κ B (NF-κB) (Sahu et al., 2014). NF-κB is a family of transcription factors that regulate expression of various genes involved in inflammatory, anti-apoptotic and immune responses (Hayden & Ghosh, 2008; Li & Lin, 2008), and its continuous activation is important for cancer development and progression (Inoue et al., 2007). Thus, it is reasonable to speculate that HNRNPA1 might somehow facilitate the development and progression of cancer. In 85% of tumors, stabilized telomeres are thought to be a direct consequence of the reactivation of the telomerase (Kim et al., 1994). Recently, some studies demonstrated that HNRNPA1 is overexpressed in multiple human cancers, including breast (Li et al., 2009), oligodendrogliomas (Xu et al., 2001), chronic myelogenous leukemia (Iervolino et al., 2002), colon (Ma et al., 2009) and hepatocellular (Zhou et al., 2013). A previous study showed that reducing HNRNPA1 by small interfering RNA induced apoptosis in cell lines derived from cervical, colon, breast, ovarian, and brain cancers (Patry et al., 2003). Enhanced expression of HNRNPA1 is correlated with the increasing severity of colorectal tissue and the progression of the colorectal cancer, as well as recurrence and decreased survival (Ma et al., 2009). For hepatocellular carcinoma, HNRNPA1 overexpression promotes tumor invasion through regulating CD44v6 and

Abbreviations: HNRNPA1, Heterogeneous nuclear ribonucleoprotein A1; IκBα, inhibitory subunit of nuclear factor κ B alpha; RNAi, RNA interference; NSCLC, non-small cell lung cancer; TKIs, tyrosine kinase inhibitors; NF-κB, nuclear factor κ B; shRNA, short hairpin RNA; IHC, immunohistochemistry; FFPE, formalin-fixed paraffin-embedded; HEK293T cell line, Human embryonic kidney 293 T cell line; FBS, fetal bovine serum; GFP, green fluorescent protein; scr-shRNA, scrambled shRNA; qPCR, Quantitative real-time polymerase chain reaction; MTT, 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2-H-tetrazolium bromide; OD, optical density.

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indicates poor prognosis (Zhou et al., 2013). However, the role of *HNRNPA1* in lung cancers has not yet been determined.

The present study aims to explore the role of HNRNA1 in lung cancers. First,we found that HNRNPA1 protein is aberrantly overexpressed in specimens of lung adenocarcinoma as compared to adjacent normal tissues. Then we used short hairpin RNA (shRNA) to downregulate the expression of HNRNPA1 in A549 lung cancer cell line. The results showed that reduction in HNRNPA1 expression inhibited cell proliferation and induced cell cycle arrest in G0/G1 phase. Our work demonstrated that *HNRNPA1* might play an important role in human lung cancer progression.

2. Materials and methods

2.1. Collection of clinical specimens

Ninety-six formalin-fixed paraffin-embedded (FFPE) lung adenocarcinoma samples were collected for this study. All the samples were used with the written informed consent from patients and the approval of the ethic committee.

2.2. Immunohistochemistry (IHC) staining

Immunohistochemistry staining for HNRNPA1 was performed in lung adenocarcinoma tissues and corresponding para-cancerous tissues as described previously (Gu et al., 2013). The slides were deparafinized, rehydrated, then immersed in 3% hydrogen peroxide solution for 10 min, heated in citrate buffer, pH 6.0, at 95 °C for 25 min, then cooled at room temperature for 60 min. The slides were blocked by 10% normal goat serum at 37 °C for 30 min, and then incubated with rabbit polyclonal antibody against HNRNPA1(diluted 1: 200, Sigma, USA) for overnight at 4 °C. After washing with PBS, the slides were incubated with biotionylated second antibody (diluted 1: 100, Sigma, USA) for 30 min at 37 °C, followed by streptavidin-peroxidase (1: 100 dilution) incubation at 37 °C for 30 min. Immunolabeling was visualized with a mixture of DAB solution. Counterstaining was carried out with hematoxylin.

The slides were evaluated in a double-blind manner by three pathologists independently. In brief, 5 randomly selected high-power fields per sample were chosen at random, and staining density of HNRNPA1 was scored and divided into 4 different types as 0 (−, no staining), 1 (+, faint reactivity without any background staining), 2 (++, moderate reactivity) and 3 (+++, granular reactivity of strong intensity in 10% of tumor cells).

2.3. Cell Culture

Human embryonic kidney 293 T (HEK293T) cell line and human lung cancer cell line A549 were obtained from the Cell Bank of Chinese Academy of Sciences (Shanghai, China). Cells were maintained in Dulbecco's modified Eagle's medium (Hyclone, Logan, UT, USA) supplemented with 10% fetal bovine serum (FBS) in a 5% CO_2 incubator at 37 °C.

2.4. Construction of recombinant lentivirus and gene silencing

The shRNA sequence (5′-GCCACAACTGTGAAGTTAGAACTCGAGT TCTAACTTCACAGTTGTGGCTTTTT-3′) and(5′-CGAAGTGGTTCTGGAA ACTTTCTCGAGAAAGTTTCCAGAACCACTTCGTTTTT-3′) for *HNRNPA1* (NM_002136.2) was selected after screening to validate potential siRNAs. Scrambled shRNA (5′-GCGGAGGGTTTGAAAGAATATCTCGA GATATTCTTTCAAACCCTCCGCTTTTTT-3′) was used as control. shRNA targeting *HNRNPA1* and control shRNA were respectively cloned into pGCSIL-GFP plasmid vector (Shanghai Hollybio, China) which contains green fluorescent protein (GFP) gene as a reporter with an internal CMV promoter. *HNRNPA1* –shRNA and scrambled shRNA (scr-shRNA) contained plasmids were prepared and confirmed by DNA sequencing. The *HNRNPA1* -shRNA (or Scr-shRNA contained) plasmid, pVSVG-I and pCMV△R8.92 (Shanghai Hollybio, China), were transfected into 293 T cells based on the instruction of Lipofectamine 2000 (Invitrogen, Carlsbad, CA,USA) when the cell density reached 70–80%.Lentivirus particles expressing *HNRNPA1*-shRNA or scr-shRNA, termed *shHNRNPA1* or shCon, were harvested after 48 h culture. A549 cells (5 × 104 cells/well) were seeded into 6-well plates and transduced with shRNPA1 and shCon, respectively.

2.5. Western blot analysis

After infection for 7 days, cells were collected and suspended in a lysis buffer(100 mM Tris–Hcl (pH 6.8), 10 mM EDTA, 4% SDS, 10% Glycine). 8% SDS/PAGE was used, and 30 μg of protein in each lane was separated by 8% SDS/PAGE (Sangon Biotech, Shanghai, China) and transferred to the PVDF membrane (Amersham, UK). After blocking of the nonspecific binding sites for 1 h with 5% nonfat milk (Guang Ming, Shanghai, China) in NaCl/Tris-Tween (Sangon Biotech, Shanghai, China) at room temperature, the membranes were incubated with primary antibodies overnight at 4 °C. Then, the membranes were subjected to three 5-min washes with NaCl/Tris-Tween (Sangon Biotech, Shanghai, China), and incubated with horseradish peroxidase-conjugated secondary antibody for 2 h at room temperature. Proteins were visualized on an ECL plus (Amersham, UK) Western blotting detection.

The antibodies used were as follows: anti-HNRNPA1 (1:4000 dilution; Sigma, USA), anti-GAPDH (1:40,000; Proteintech Group, Inc.) HRP-conjugated goat anti-rabbit IgG (H&L) antibody and goat anti-mouse IgG (H&L) antibody (1: 5000 dilution; Santa-Cruz Biotechnology).

2.6. Quantitative real-time polymerase chain reaction (qPCR)

Total cellular RNA was extracted using TRIzol reagent (Invitrogen) and reversely transcripted to cDNA by M-MLV reverse transcriptase (Promega Corp.) according to the manufacturer's instructions. qPCR products were detected with SYBR Green I dye by using Biorad Real Time System (Biorad, USA). Actin gene was amplified as internal control. The primer sequences used were as follows: Actin-forward, GTGGACATCCGCAAAGAC; Actin-reverse, AAAGGGTGTAACGC AACTA; *HNRNPA1*-forward, ACGAAACCAAGGTGGCTATG, *HNRNPA1*-reverse, GTGCTTGGCTGAGTTCACAA. Relative quantitation was done by taking the difference[Delta C(T)] between the C(T) of Actin and C(T) of each gene and computing 2[−Delta Delta C(T)].

2.7. 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2-H-tetrazolium bromide (MTT) cell proliferation assay

Lentivirus-shRNA infected cells at the logarithmic phase were seeded into 96-well plates at the density of 2500 cells/well, and were incubated in 5% CO_2 incubator at 37 °C. After one, two, three, four days of culture, the cell viability was assessed by MTT assay. Briefly, 20 uL of MTT (5 mg/mL) was added and incubated for four hours. The reaction was terminated by removal of the supernatant and addition of 100uL of DMSO. The optical density (OD) of each well was measured at 595 nm using ELISA reader.

2.8. Colony formation assay

Lentivirus-infected cells at the logarithmic phase were inoculated in six-well plates at the density of 400 cells/well. Culture medium was changed every three days. When the cell number in most single colony was over 50, cells were fixed for 30 min in paraformaldehyde (Sangon Biotech Shanghai Co.Ltd), washed with PBS and stained with Crystal purple. After washing with ddH_2O, the number of colonies was counted under the fluorescence microscope (Olympus, CKX41).

2.9. Flow cytometry assay

After lentivirus infection treatment, cells in each well were harvested and cell cycle distribution was determined by flow cytometry using PI staining method. Tests were performed in triplicate for each sample, and analyses were performed by FACS can flow cytometer (Becton Dickinson, San Jose, CA, USA) in accordance with the manufacturer's guidelines.

2.10. Statistical analysis

All data were presented as mean ± SD of at least independent experiments. The statistical difference of HNRNPA1 expression between in human lung adenocarcinoma tissue and adjacent normal tissues was evaluated in a cross-table with the chi-square-test. Other results were analyzed with Student's t-test. All statistical analysis was performed with SPSS version 20.0 (SPSS, Chicago, IL, USA). A *P* value less than 0.05 is considered to be statistical significant.

3. Results

3.1. HNRNPA1 expression is aberrantly higher in lung adenocarcinoma as compared to adjacent normal tissues

As elevated HNRNPA1 expression was found in 7 types of human cancers,we first determine the expression of HNRNPA1 in lung adenocarcinoma samples and related adjacent normal tissues of 96 patients through immunohistochemistry (IHC) staining. Representative images showing either weakly positive (top panel) or strongly positive (bottom panel) HNRNPA1 were displayed in (Fig 1). Positive expression of HNRNPA1 was observed in 69.7% (67/96, including (63 + and 4 ++) lung adenocarcinoma tissues, while only in 18.8% (18/96, including 18 + and 0 ++) adjacent normal tissues (Table 1). This indicated that in lung adenocarcinoma, HNRNPA1 expression is upregulated compared to adjacent normal lung tissues. The statistical analysis showed that positive expression of HNRNPA1 in lung adenocarcinoma tissues and adjacent normal lung tissues was significantly different ($P < 0.001$). We also determined the relationship between the immunohistochemical expression level of HNRNPA1 and clinicopathologicalparameters of lung cancer patients. The results showed that positive rate of male patients is significantly higher than female patients, the other clinicopathological parameters had no effect on HNRNPA1 expression (Table 2).

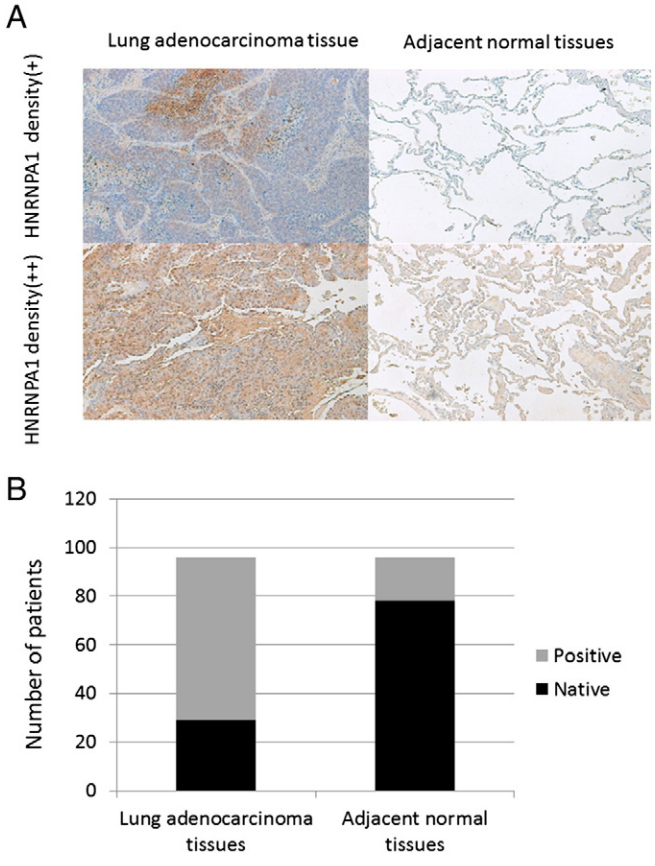

Fig. 1. Expression status of HNRNPA1 in lung adenocarcinoma patients. (A) Representative immunohistochemistry pictures showing the expression status of HNRNPA1 protein in lung adenocarcinoma tissues and adjacent normal tissues from two patients. Weakly positive MFN2 signal was detected in Patient 1(top panel), while strongly positive HNRNPA1 signal was detected in Patient 2(bottom panel). (B)Quantification of HNRNPA1 protein expression status in lung adenocarcinoma tissues and adjacent normal tissues by IHC staining (n = 96).

Table 1
HNRNPA1expression density in lung adenocarcinoma and adjacent tissues by immunohistochemistry (IHC) staining.

	Case number	Expression status of HNRNPA1		P *value**
		Negative (−)	Positive (+, ++)	
Lung adenocarcinoma tissues	96	29	67	< 0.001
Adjacent normal tissues	96	18	78	

*P value of the comparison was conducted by Pearson χ^2.

3.2. Lentivirus-mediated HNRNPA1 knockdown effectively and particularly reduced HNRNPA1 mRNA and protein expression in A549 Cells

The two shRNA for *HNRNPA1* were named shVL273 and shVL274 respectively.To determine the lentiviral transduction efficiency in A549 cells, GFP expression was examined by microscope after 4 day infection, as shown in Fig. 2A. qPCR and Western blot were then utilized to detect the expression level of *HNRNPA1* after lentivirus infection for four days and seven days respectively. Compared with shCon group, the mRNA level of *HNRNPA1* in both of *shHNRNPA1* groups was significantly decreased (P < 0.01) (Fig.2B, D). Moreover, expression of HNRNPA1 protein was also significantly inhibited in *HNRNPA1* knock-down A549 cells (Fig.2C, E), indicating that lentivirus-mediated knockdown of *HNRNPA1* could effectively impair the expression of *HNRNPA1* in lung cancer cells.

3.3. Effect of HNRNPA1 down regulation on proliferation of A549 cells

To further evaluate whether *HNRNPA1* silencing in A549 cells might inhibit cell growth and proliferation, MTT and colony formation assays

Table 2
Relationship between clinicopathological parameters and HNRNPA1 immunohistochemical expression.

Clinicalpathological parameters	Num	HNRNPA1 expression		X^2	*P*- value
		Negative,case, of NO(%)	Positive,case, of NO (%)		
Age(years)				1.786	0.181
<60	53	19(35.8)	34(64.2)		
≥60	43	10(23.3)	33(76.7)		
Gender				8.758	0.003
Male	58	11(19.0)	47(71.0)		
Female	38	18(47.4)	20(52.6)		
TNM stage				0.258	1.000
I + II	5	1(20.0)	4(80.0)		
III + IV	91	28(30.8)	63(69.2)		

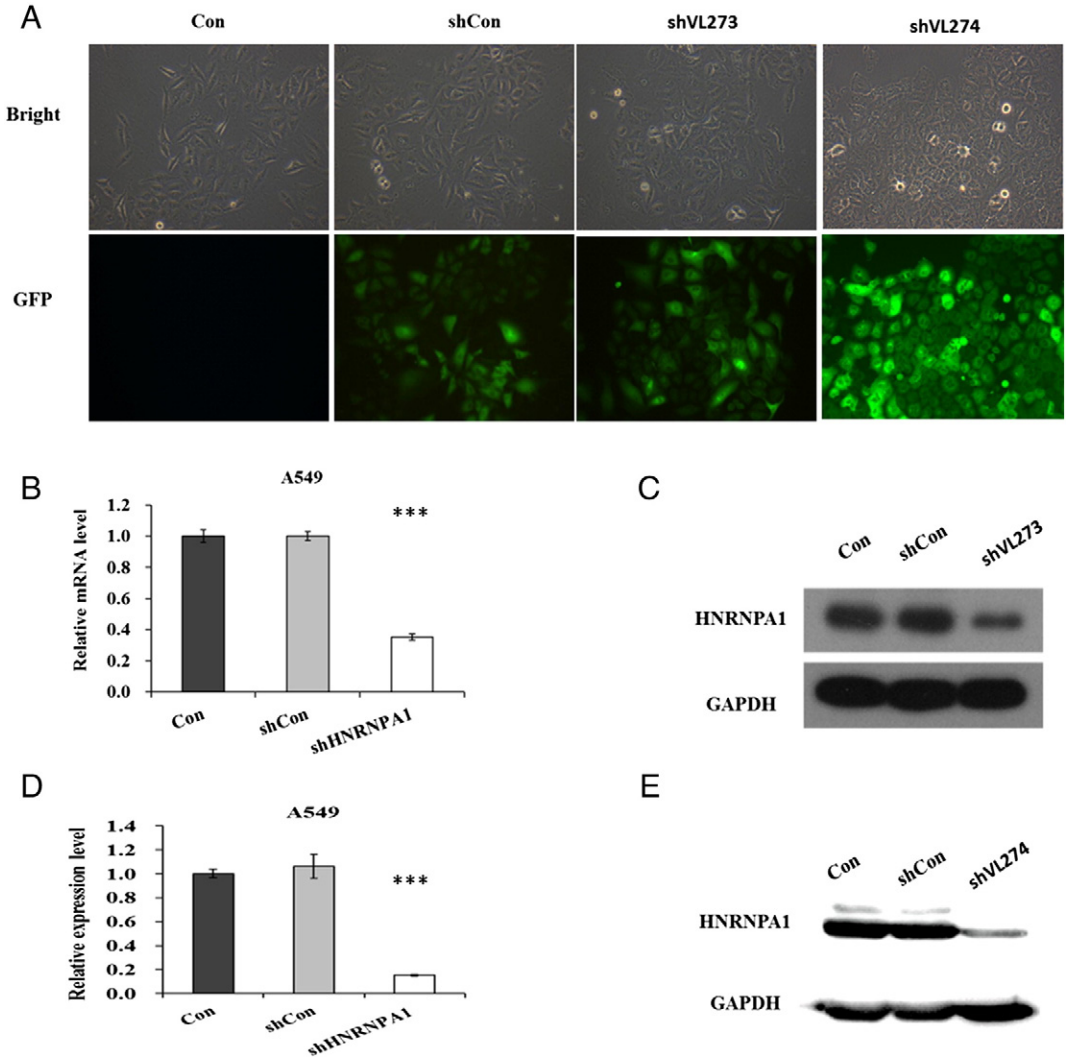

Fig. 2. Lentivirus-mediated shRNA decreased HNRNPA1 expression in A549 cells. (A) Lentivirus transduction efficiency was estimated after A549 cells infected with shVL273 and shVL274 or shCon 3 days. GFP expression in transfected cells was observed under a light microscope(upper) and a fluorescence microscope(lower). Magnification:100. (B) Expression levels of mRNA were measured by qPCR. In comparison with shCon group, shVL273 and shVL274 lentivirus infection resulted in 64.7% and 85.7% decrease in the expression level of HNRNPA1 mRNA in A549 cells, ***$P < 0.001$.(C) Expression level of HNRNPA1 protein in A549 cells with Western blot. HNRNPA1 protein was significantly downregulated in shHNRNPA1lentivirus infected A549 cells. Con, uninfected cells; shCon, cells infected with non-silencing shRNA; shVL273, cells infected with HNRNPA1 shVL273.; shVL274, cells infected with HNRNPA1 shVL274.

were performed. The number of viable cells was detected by MTT assay daily for 5 days. As shown in Fig.3A.B, cell viability of A549 cells was significantly inhibited compared with the shCon group ($P < 0.001$).

Furthermore, in the colony assay, cells in the shCon group were in cluster growth and formed lots of colonies after 14 days infection, but the colony formation was almost completely inhibited in *HNRNPA1* knock-down cell line (Fig. 4A). Compared with the shCon group, the number of colony in *shHNRNPA1* group cells was decreased by 87.5% ($P < 0.001$, Fig.4B), unearthing that knockdown of *HNRNPA1* weakened the proliferation of lung cancer cells.

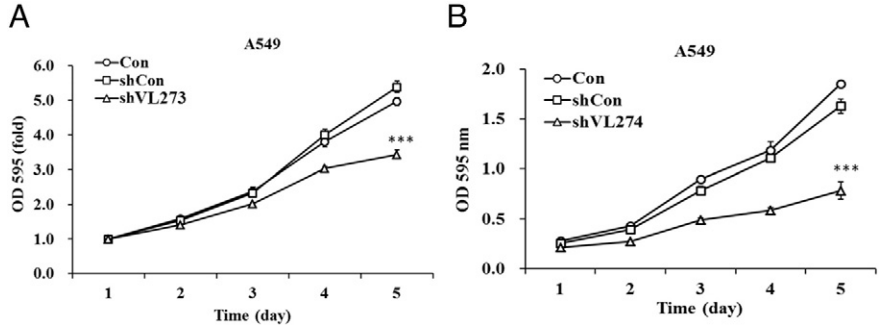

Fig. 3. The effect of HNRNPA1 knock down on the proliferation of lung cancer cells. (A) Analysis of cell viability of shVL273 lentivirus or shCon lentivirus infected cells for one to five days. In compared with the Con or shCon group,the proliferation of A549 cells was significantly inhibited after HNRNPA1 knock down, ***$P < 0.001$.(B) Analysis of cell viability of shVL274 lentivirus or shCon lentivirus infected cells for one to five days. The proliferation of A549 cells was significantly inhibited after HNRNPA1 knock down too, ***$P < 0.001$.

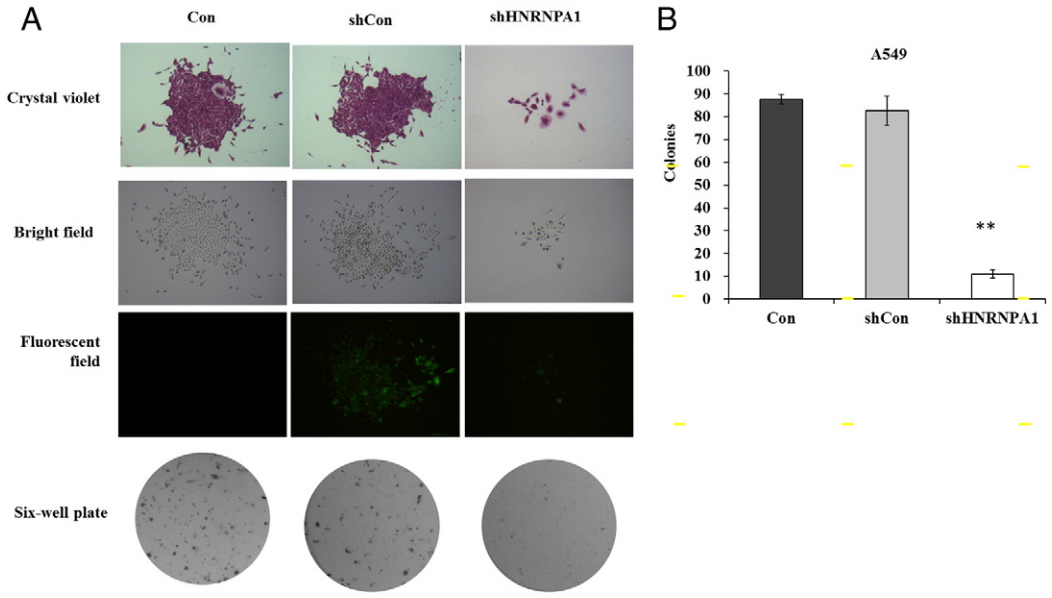

Fig. 4. The effect of HNRNPA1 knock down on the colony formation of lung cancer cells. (A) The colony formation of A549 cells in Con, shCon and shHNRNPA1 group was asssayed after 10 days culture. (B) Statistical results of colony number showed that the colony-forming ability was impaired in shHNRNPA1 lentivirus infected A549 cells, $^{***}P < 0.001$.

3.4. Downregulation of HNRNPA1 induced cell cycle arrest at G0/G1 phase

To explore the possible underlying mechanisms of *HNRNPA1* suppression in inhibiting A549 cell proliferation, the effect of *HNRNPA1* silencing on cell cycle progression was analyzed by flow cytometry (Fig.5A). The results uncovered that knockdown of *HNRNPA1* in A549 cells induced an increase in the percentage of cells in G0/G1 phase (from 58.5% in the shCon group to 69.1% in the shRNPA1 group, $P < 0.01$), paralleling with a decrease in the percentage of cells in S phase (from 28.1% in the shCon group to 20.1% in the shRNPA1 group, $P < 0.01$) (Fig.5B). All these results demonstrated that *HNRNPA1* knockdown inhibited cell viability and proliferation of A549 cells might through G0/G1 cell cycle arrest.

4. Discussion

Identification of targets that are specifically expressed in cancer cells and also play an important role in promoting or allowing unlimited cell division is the key for tumors treatment. At the present, targeted therapies against known genes or pathways in lung adenocarcinoma have improved patient prognosis obviously (Mok et al., 2013). But, it is urgent to explore more novel genes or biomarkers involved in lung adenocarcinoma. Here, we present evidence that the *HNRNPA1* may have an important role in human lung adenocarcinoma.

Indeed,a previous study reported that the transcription level of *HNRNPA1* was frequently upregulated in A549 cell lines (Romero-Garcia et al., 2014). This is consistent with our study, what's more, in our study we used 96 specimens to quantify HNRNPA1 expression status and proved that HNRNPA1 protein was overexpressed in lung adenocarcinoma tissues. Another study reported that reduction in A1/A2 proteins in a variety of human cell lines derived from cervical, colon, breast, ovarian, and brain cancers provoked specific and rapid cell death by apoptosis in cell lines and a reduction in A1 alone or in A2 alone did not promote cell death (Patry et al., 2003). So they said combined reduction of hnRNP A1/A2 was a potential strategy of cancer treatment. We employed shRNA to specifically decrease the expression of HNRNPA1 in A549 cancer cells. Then we measured the cell viability and proliferation through MTT and colony formation assay, and found A549 cell viability and colony formation was significantly inhibited. In addition, the decrease in cell viability and proliferation partly attributed to the occurrence of G0/G1 cell cycle arrest. This means drugs targeting HNRNPA1 alone can be also used in lung adenocarcinoma therapeutics.

Cell cycle is a highly regulated process and one of the most crucial steps is chromosome replication. The telomeres are essential for protecting chromosome ends from degradation, recombination, and fusion events. An absence of telomerase can lead to a gradual loss of telomere sequence and eventual cell division arrest (Karlseder et al., 2002). Current cancer models for human cells postulate most of the tumors get stabilized telomeres through reactivation of the telomerase enzyme as a result of gene mutation (Harley et al., 1994; Kim et al., 1994; de Lange & Jacks, 1999). Many studies show inactive telomerase in human cancer cells lead to grow arrest and cell death (Herbert et al., 1999; Hahn et al., 1999; Feng et al., 1995). *HNRNPA1* can interact simultaneously with telomerase RNA in vitro (Fiset & Chabot, 2001)and defective HNRNPA1 expression in mouse erythroleukemic cells results in short telomeres, which can be lengthened by restoring normal level of *HNRNPA1* (LaBranche et al., 1998). Reduction in *HNRNPA1* induces apoptosis in cervical cancer cells but not in normal mortal cell lines (Patry et al., 2003). So, knockdown *HNRNPA1* might break the stability of telomeres in A549 cells, thus prevent the growth of cancer cells.

The NF-κB family of transcription factors consists of five members named p50, p52, RelA (also known as p65), RelB and c-Rel and regulates expression of various genes involved in inflammatory, anti-apoptotic and immune responses (Hayden & Ghosh, 2008). The activation of NF-κB in cancer cells or in stromal cells that surround tumors and constitute the tumor microenvironment promotes cancer development and progression (Inoue et al., 2007). Now, NF-κB has been thought to be a target for cancer therapy (Brown et al., 2008; Melisi & Chiao, 2007; Luqman & Pezzuto, 2010). The basic scheme of NF-κB signaling consists of a series of positive and negative regulatory elements. When NF-κB complexes remain in the cytoplasm, they are inhibited by an inhibitory molecule of the IκB family. In mammalian species, IκB family consist of seven members: IκBα, IκBβ, IκBγ, IκBε,IκBζ, IκBNS and Bcl-3 (Tucker et al., 2012). Recently, a study demonstrates that *HNRNPA1* is involved in enhancing IκBα degradation and NF-κB activation (Sahu et al., 2014). Thus, we can hypothesize reduction of *HNRNPA1* leads to decrease of IκBα degradation, resulting in inactivation of NF-κB. And NF-κB inactivation will inhibit cancer cells proliferation, consistent with our study.

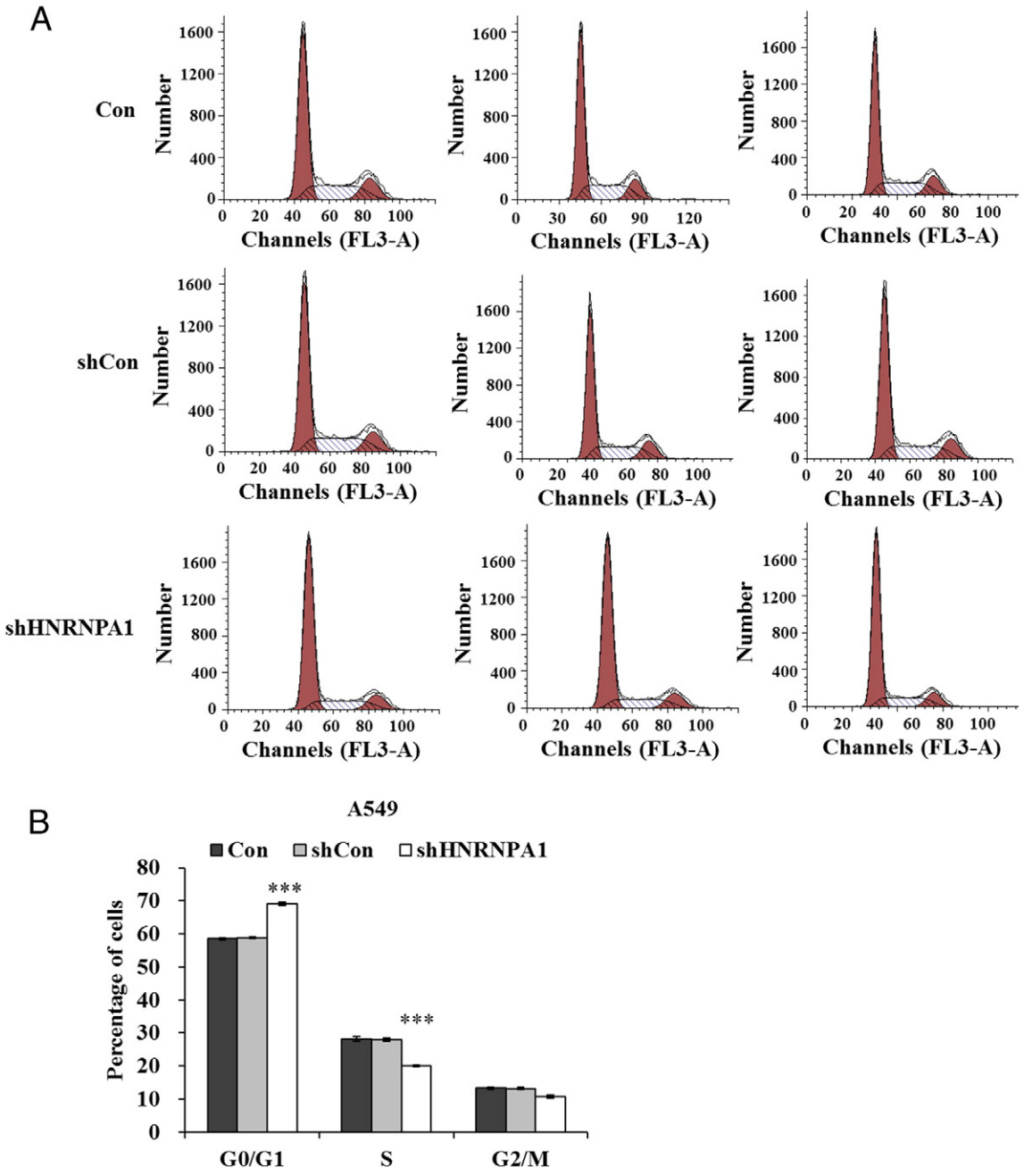

Fig. 5. Flow cytometric analysis of cell cycle distribution in A549 cells (A) Knockdown of HNRNPA1 by RNA interference in A549 cells induced cell cycle arrest in G0/G1 phase at 5 days after lentivirus transduction. (B) Percentage of cells under different stages of G0/G1, S, G2/M phase. ***$P < 0.001$, compared to shCon.

Our results firstly showed that HNRNPA1 aberrantly overexpressed in lung adenocarcinoma and then lentivirus-mediated RNA interference effectively and specifically suppressed HNRNPA1 expression in A549 cells. We found the reduction of *HNRNPA1* significantly inhibited A549 cells proliferation partly by inducing cell cycle arrest in G0/G1 phase, possibly acting by affecting the expression of telomerase and NF-κB activation. Further researches are needed to illuminate the detailed mechanism of HNRNPA1 in lung cancer. Our study demonstrates that HNRNPA1 might be a promising target for lung adenocarcinoma therapy.

Conflict of interest

The authors declare that they have no conflict of interest.

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