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Long noncoding RNA ABHD11-AS1 predicts the prognosis of pancreatic cancer patients and serves as a promoter by activating the PI3K-AKT pathway

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Abstract. – OBJECTIVE: Accumulating evidence showed aberrant expressions of long non-coding RNAs (lncRNAs) strongly correlated to the development of cancers, including pancreatic cancer (PC). Whether lncRNA ABHD11-AS1 (ABHD11-AS1) is involved in PC remains to be elucidated. Thus, we aimed to evaluate the effects of ABHD11-AS1 on PC and the underlying molecular mechanism.

PATIENTS AND METHODS: RT-PCR was used to detect the expression level of ABHD11-AS1 in both PC tissue and cell lines. Then, the correlation of ABHD11-AS1 expression with clinicopathological features and prognosis was studied. Cell proliferation, apoptosis, migration and invasion abilities were detected by MTT, flow cytometry, and transwell assays. We further investigated the effect of abnormal ABHD11-AS1 expression through the PI3K/AKT and EMT pathway by Western blot assays in treated PC cells.

RESULTS: We found that the expression of ABHD11-AS1 was significantly increased in both PC tissues and cell lines. The clinical analysis revealed that a high level of ABHD11-AS1 expression was correlated with distant metastasis, TNM stage, and tumor differentiation. The Kaplan-Meier analysis showed that high ABHD11-AS1 expression levels predicted poorer survival. Moreover, univariate and multivariate analyses confirmed that the expression of ABHD11-AS1 was an independent and significant factor associated with poor overall survival rates. Loss-of-function experiments showed that the knockdown of ABHD11-AS1 suppressed PC cell proliferation, migration, invasion, and EMT *in vitro.* Mechanistically, the knockdown of ABHD11-AS1 decreased phospho(p) AKT and phospho(p) PI3K expression, but did not affect the AKT and PI3K expression in PC cells

CONCLUSIONS: This study suggested that ABHD11-AS1 may potentially function as a valuable prognostic biomarker and a therapeutic target for PC patients.

Key Words:
Long noncoding RNA, ABHD11-AS1, PI3K/AKT pathway, Prognosis, Pancreatic cancer.

Introduction

Pancreatic cancer (PC) is one of the most lethal human malignancies, and its incidence appears to increase[1]. In China, PC has been the sixth high mortality reason among cancer-related diseases[2]. Despite a large number of efforts and improvements in surgery and perioperative management, the survival rate of advanced PC has not improved over the past decades[3,4]. The poor survival is due to the lack of early diagnosis and no effective therapeutic method once metastasis has occurred[5]. Therefore, the research on the molecular mechanisms underlying the oncology of PC is of clinical significance for promoting early diagnosis, predicting the prognosis and

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developing novel therapeutic strategies for PC. Long non-coding RNAs (LncRNAs) are over 200 nucleotides in length without protein-coding capacity[6]. It has been reported that lncRNAs may be implicated in various types of gene regulation, including transcriptional, post-transcriptional or epigenetic regulation[7]. Growing evidence indicates that lncRNAs are widely expressed in human cells and act as critical regulators in various biological events, such as proliferation and differentiation, apoptosis and cell cycle[8,9]. In addition, it is well recognized that some altered expression of lncRNAs has been frequently linked with cancer pathogenesis[10,11]. For instance, LncRNA SNHG12 was highly expressed in lung cancer and its knockdown inhibited lung cancer cells proliferation by upregulating miR-138[12]. Liu et al[13] found that lncRNA ZEB1-AS1 was up-regulated in osteosarcoma and associated with advanced clinical stages as well as poor prognosis. *In vitro* experiments showed that enhanced expression of lncRNA ZEB1-AS1 promoted osteosarcoma cells proliferation and migration by epigenetically activating ZEB1. However, the expression, clinical significance and biological function of lncRNAs remain largely unclear. LncRNA ABHD11 antisense RNA1 (ABHD11-AS1), located at human chromosome 7 q11. 23, was a newly identified lncRNA. Previous studies have reported that ABHD11-AS1 was dysregulated in several tumors, including gastric cancer[14], bladder cancer[15], endometrial carcinoma[16] and epithelial ovarian cancer[17]. However, whether ABHD11-AS1 was abnormally expressed and its biological function in PC have not been investigated. The present work will provide new insights into the biological functions of ABHD11-AS1 as well as its regulatory mechanisms of targets in PC.

Patients and Methods

Patients and Samples

Surgically resected paired pancreatic tumor tissue samples and corresponding non-cancerous tissue samples were collected from patients with PC at the Department of Gastroenterology, The Affiliated Huaian Hospital of Xuzhou Medical University between April 2010 and July 2013. All samples were diagnosed correctly based on clinical and pathological evidence. None of the patients had received preoperative radiation or chemotherapy. Clinical data and follow-up records of PC patients were collected in a dedicated electronic database. All tissues were immediately snap-frozen in liquid nitrogen and stored at -80°C until further studies. The clinicopathological information of the patients was in Table II. Patients signed an informed consent and the study was approved by the Ethical Committee for Clinical Research of the Hospital.

Cell Lines and Cell Culture

Human PC cell lines (Capan-2, L3.6pl, BxPC3, AsPC-1 and PANC-1) and pancreatic cell line HPDE6-C7 were purchased from the Type Culture Collection of the Chinese Academy of Sciences (Xuhui, Shanghai, China). All cell lines were maintained in Roswell Park Memorial Institute-1640 medium (RPMI-1640; Gibco, Grand Island, NY, USA) supplemented with 10% fetal bovine serum (FBS; Gibco, Grand Island, NY, USA) and 1% penicillin/streptomycin (Pudong, Shanghai, China) in humidified air containing 5% CO_2 at 37°C.

Cell Transfection

The siRNA control (siControl), ABHD11-AS1 siRNA1 (siRNA1) and ABHD11-AS1 siRNA2 (siRNA2) were synthesized by GenePharma Biotechnology Co., Ltd.(Shanghai, China). SiRNA transfections were performed using Lipofectamine 3000 (Life Technologies, Gaithersburg, MD, USA). Briefly, L3.6pl and PANC-1 cell lines were seeded into six-well plates (Corning Incorporated, Shanghai, China) at 2×10^5 cells per well. After the cells reached 70% confluence, 16 μl of Lipofectamine 3000 reagent was mixed with 12 μl siRNA duplex (20 μM) in the Opti-MEM (Invitrogen, Carlsbad, CA, USA) and the complexes were then added into the cultured cells. After 12 h incubation, the medium was replaced with fresh RPMI-1640 medium containing 10% FBS.

RNA Extraction and Real Time-Quantitative RT-PCR (qRT-PCR)

Total RNA from PC tissues and cell lines was isolated from cells using TRIzol Reagent (Beyotime, Shanghai, China). The first-strand cDNA was reversely transcribed from 10 ng total RNA using TransScript Fly First strand cDNA Synthesis SuperMix. Subsequently, qPCR was carried out by TransStart Green qPCR SuperMix (TransGen Biotech, Beijing, China) and the Applied Biosystems 7500 Fluorescent Quantitative PCR system (Applied Biosystems, Foster City, CA, USA). The internal control for cell lines experiments used in this study was glyceraldehyde-3-phosphate dehydrogenase (GAPDH). All

the primer sequences were listed in Table I. The relative expression fold change of ABHD11-AS1 was calculated by the $2^{-\Delta\Delta CT}$ method.

Western Blot Analysis

Cells were harvested and lysed by RIPA buffer (Sigma-Aldrich, St. Louis, MO, USA) with protease inhibitor cocktail (Pierce Biotechnology, Waltham, MA, USA). Subsequently, the proteins were separated by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and transferred to polyvinylidene difluoride (PVDF) membranes (Millipore, Billerica, MA, USA). The membranes were blocked with 5% skimmed milk for 1 h and incubated with primary antibodies: anti-Vimentin antibody, anti-E-Cadherin, anti-p-PI3K, anti-PI3K, anti-AKT, anti-p-AKT antibody, anti-GAPDH antibody. Subsequently, the membrane was incubated with secondary antibodies at 37° C while shaking on a rotary for 2 h. Then, the detection was performed by enhanced chemiluminescence (ECL) kit (Beyotime, Shanghai, China). Quantity One Software (Bio-Rad, Hercules, CA, USA) was used to analyze the intensity of blots.

Cell Proliferation Assay

Cell proliferation was evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay (Sangon, Shanghai, China). Briefly, cells were seeded into 96-well plates at a density of 1000 cells per well in triplicate and subsequently incubated for 24 h to 72 h after siRNA transfection. Then, 20 µl MTT solution was added into each well and cultured at 37° C. After the supernatant was discarded, dimethyl sulfoxide (100 µL/well) was added into each well and the absorbance was measured at 490 nm using a spectrophotometer (BioTek, Winooski, VT, USA). MTT assay data were calculated relative to day 1.

Colony Formation Assay

Cells from different groups were seeded into 6 cm dishes (1000 cells/wells) accordingly. After culturing for about 2 weeks, the cell colonies were fixed by 4% paraformaldehyde and further stained by crystal violet solution (Beyotime, Shanghai, China). Finally, the images were captured by a microscope (Nikon, Tokyo, Japan). Experiments were performed in triplicate.

Table I. The primer sequence of ABHD11-AS1 and GAPDH.

Gene	Sequence
ABHD11-AS1 (F)	5'-GAACGGGATGAAGCCATTG-3'
ABHD11-AS1 (R)	5'-GCTGATTCTGGACCTGCTG-3'
GAPDH (F)	5'-CTGGGCTACACTGAGCACC-3'
GAPDH (R)	5'-AAGTGGTCGTTGAGGGCAATG-3'

Wound-Healing Migration Assay

Cell suspensions (70 µl, 5×10^5 cells/ml) of PANC-1 and L3.6pl PC cells were added into each reservoir of the 35 mm high culture µ-dish and the cells were incubated overnight at 37°C. At about 100% cell confluence, the inserts were removed to leave a gap between the two cell layers and the medium was then replaced. Subsequently, images were captured by an inverted microscope (Nikon, Tokyo, Japan) at 0 h and 24 h.

Transwell Invasion Assay

The upper chambers of transwell inserts (8 µM pore size) (Corning, Corning, NY, USA) were coated with Matrigel (BD Biosciences, Franklin Lakes, NJ, USA) for the invasion assay. Then, the cells (200 µl; 2.5×10^5 cells/ml) were seeded in the upper chamber containing a serum-free medium. The bottom chamber was then added with 600 µl medium supplemented with 10% FBS. After 16 h incubation at 37˚C, the upper surface of the membrane was wiped. The cells located on the lower surface of the chamber were fixed in 90% ethanol (Sangon, Shanghai, China) and stained by crystal violet solution (Beyotime, Shanghai, China).

Flow Cytometry Analysis of Apoptosis

Apoptosis assay was performed using an Annexin V-fluorescein isothiocyanate (FITC) apoptosis detection kit (Invitrogen, Carlsbad, CA, USA). In short, cold PBS-washed PANC-1 and L3.6pl PC cells were stained using Annexin V-FITC/propidium iodide (PI) regents. Then, the cells were incubated for 30 min at room temperature in the dark and FACS Calibur flow cytometry was employed to determine the number of apoptotic cells.

Statistical Analysis

Data were analyzed using SPSS 16.0 software (statistical package for the Social Sciences Version 16.0, SPSS Inc., Chicago, IL, USA). The differences were evaluated by one-way ANOVA or Student's *t*-test. Tukey post-hoc test was performed to analyze the difference among three or above groups. The relationships between

ABHD11-AS1 expression and clinicopathological parameters were examined by the chi-square test. The overall survival (OS) was estimated by using the Kaplan-Meier method. The cox proportional hazards model was used to estimate the survival in univariate and multivariate analyses. $p < 0.05$ was considered to be statistically significant.

Results

ABHD11-AS1 Was Up-Regulated in Patients With PC

We first identified differentially expressed genes using "GEPIA" which is an online bioinformatics tool for genes expression analysis[18]. As shown in Figure 1A, we found that the expression level of ABHD11-AS1 was higher in PC tissues compared to the non-tumor tissues. In addition, the survival analysis indicated that high ABHD11-AS1 expression had a significant impact on overall survival ($p = 0.034$, Figure 1B) and disease-free survival ($p = 0.019$, Figure 1C). Then, we further analyzed the levels of ABHD11-AS1 in both PC tissues and matched normal pancreatic tissues from our hospital. Our results indicated that the levels of ABHD11-AS1 were significantly higher in PC tissues compared to the corresponding non-tumor tissues (Figure 1D). Then, the relative expression levels of ABHD11-AS1 in four PC cell lines and HPDE6-C7 cell lines were detected by qRT-PCR. We also demonstrated that ABHD11-AS1 was upregulated in PC cell lines (CFPAC-1, BXPC-3, L3.6pl and PANC-1) compared to HPDE6-C7 (Figure 1E).

The Association Between ABHD11-AS1 Expression and Overall Survival of Patients With PC

Then, the relationship between ABHD11-AS1 expression and clinical features in PC patients was analyzed; we observed that a high level of

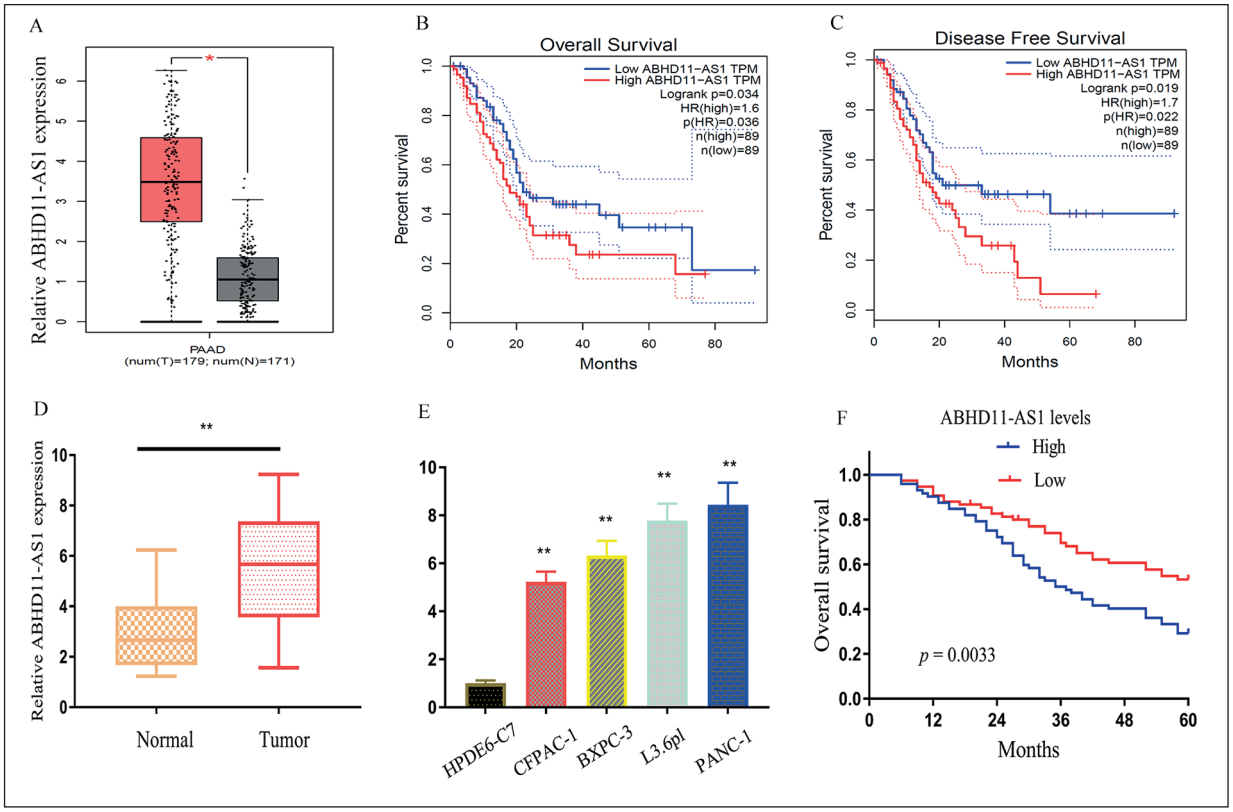

Figure 1. Relative ABHD11-AS1 expression in PC tissues and its clinical significance. ***A,*** "GEPIA" tool was used to screen abnormally expressed lncRNAs. ***B, C,*** Overall survival and disease-free survival analyzed by GEPIA based on TCGA database. ***D,*** Comparison of ABHD11-AS1 expression between PC tissues and matched normal tissues. ***E,*** qRT-PCR analysis of ABHD11-AS1 expression levels in four PC cell lines and normal cell lines (HPDE6-C7). ***F,*** Kaplan-Meier method with log-rank test was used to analyze the overall survival curves of patients in high and low ABHD11-AS1 expression groups. $*p < 0.05$, $**p < 0.01$.

Table II. Relationship between ABHD11-AS1 and clinicopathological characteristics in 147 patients with PC.

Parameters	Number of cases	ABHD11-AS1 expression		p-value
		High	Low	
Sex				NS
Male	85	41	44	
Female	62	31	31	
Age (years)				NS
< 65	73	33	40	
≥ 65	74	39	35	
Location				NS
Head, urinate	59	29	30	
Body, tail	88	43	45	
Tumor size (cm)				NS
< 2	82	35	47	
≥ 2	65	37	28	
Lymphatic invasion				NS
Positive	58	34	24	
Negative	89	38	54	
Distant metastasis				0.001
Positive	61	40	21	
Negative	86	32	54	
TNM stage				0.004
I/II	91	36	55	
III/IV	56	36	20	
Tumor differentiation				0.027
High/moderate	83	34	49	
Poor	64	38	26	

ABHD11-AS1 expression was correlated with distant metastasis (p = 0.001), TNM stage (p = 0.004) and tumor differentiation (p = 0.027). However, there were no significant correlations of ABHD11-AS1 expression with other clinical features such as age, sex, location, tumor size and lymphatic invasion (p > 0.05, Table II). Subsequently, the association between the expression levels of ABHD11-AS1 and patients' survival were assessed using Kaplan-Meier analysis with the log-rank test. As shown in Figure 1F, the results showed that the PC patients in the high ABHD11-AS1 expression group had significantly shorter 5-year OS time than those in the low ABHD11-AS1 expression group (p = 0.0033). These results were in line with previous data from online. In addition, the univariate and multivariate analysis was performed to demonstrate whether ABHD11-AS1 expression level is an independent factor for prognostic prediction in PC patients. We found that high ABHD11-AS1 expression was an independent prognostic parameter indicating poor prognosis for PC patients (Table III).

Table III. Univariate and multivariate analyses of prognostic factors in PC.

Variables	Univariate analysis			Multivariate analysis		
	RR	95% CI	p-value	RR	95% CI	p-value
Sex male *vs.* female	1.366	0.783-2.421	0.213	-	-	-
Age < 60 *vs.* ≥ 60	1.462	0.832-2.327	0.166	-	-	-
Location Head, urinate *vs.* body, tail	1.499	0.623-2.178	0.155	-	-	-
Tumor size (cm) < 2 *vs.* ≥ 2	1.773	0.891-2.673	0.169	-	-	-
Lymphatic invasion positive *vs.* negative	1.833	1.123-2.833	0.094	-	-	-
Distant metastasis positive *vs.* negative	3.667	1.563-5.294	0.002	2.933	1.267-4.563	0.005
TNM stage I/II *vs.* III/IV	3.321	1.355-4.783	0.005	2.577	1.211-3.932	0.016
Tumor differentiation high/moderate *vs.* poor	2.893	1.322-4.232	0.015	2.346	1.177-3.783	0.038
Serum LINC00899 expression high *vs.* low	4.132	1.563-6.229	0.001	3.166	1.173-4.351	0.009

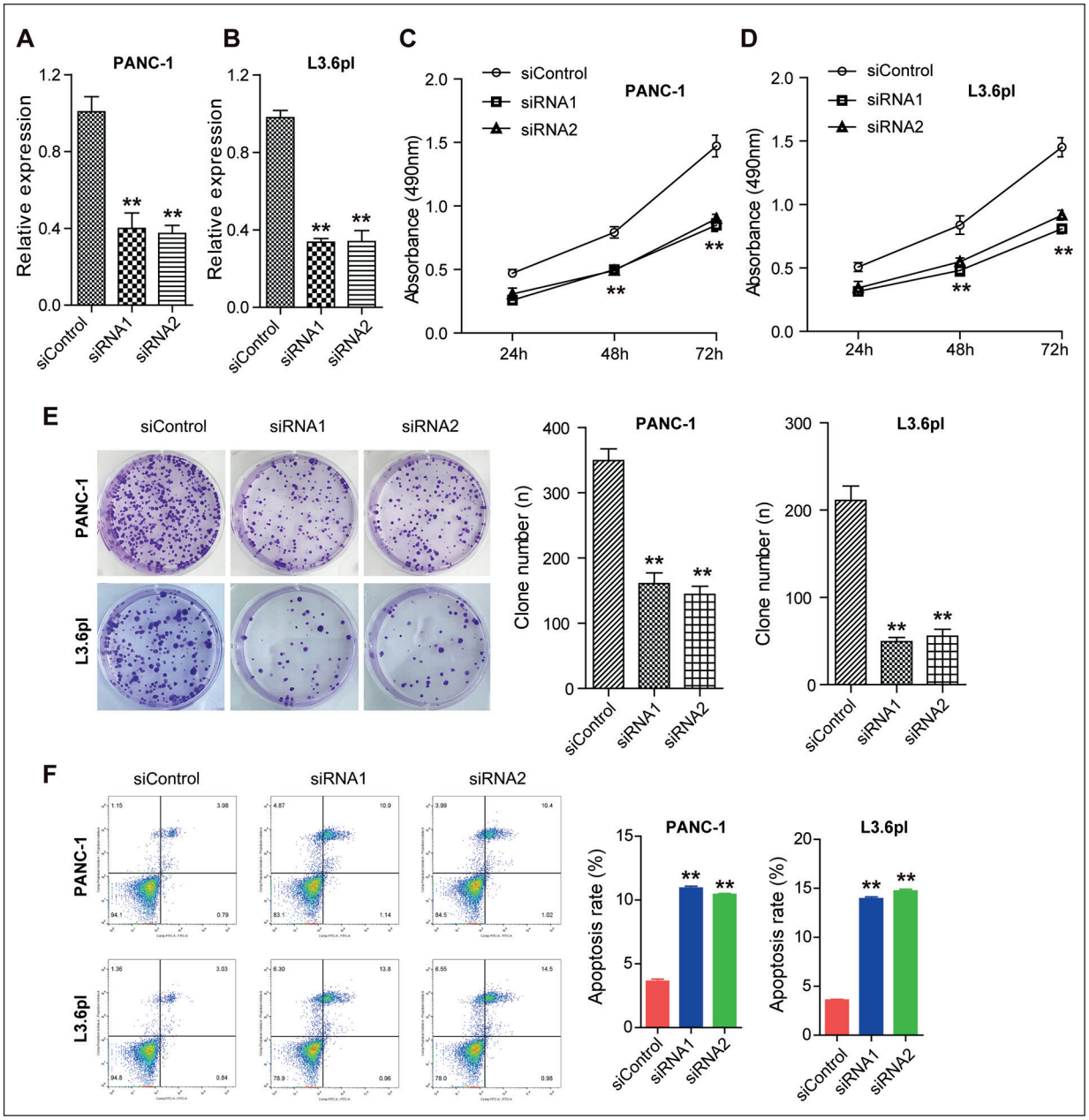

Figure 2. Effects of ABHD11-AS1 on cell proliferation and apoptosis in PANC-1 and L3.6pl cells. ***A, B,*** Relative expression levels of ABHD11-AS1 in PANC-1 and L3.6pl cells. ***C, D,*** MTT assay determined the proliferation rates of PANC-1 and L3.6pl cells. ***E,*** Colony formation assays and quantitative analysis of PANC-1 and L3.6pl cell colony number. ***F,*** Flow cytometry analysis of PANC-1 and L3.6pl cell apoptosis. The values were means ± SEM. *$p < 0.05$, **$p < 0.01$.

The Knockdown of ABHD11-AS1 Inhibited Cell Proliferation and Induced Apoptosis of PC

We next explored the effects of the altered expression of ABHD11-AS1 on cell proliferation and apoptosis in PANC-1 and L3.6pl cells lines. RT-qPCR assay suggested that ABHD11-AS1 expression was markedly downregulated in PANC-1 and L3.6pl cells transfected with siRNA1 and siRNA2 (Figure 2A, 2B). MTT assays revealed that the proliferation abilities of both PANC-1 and L3.6pl were significantly suppressed after transfection with siRNA1 and siRNA2 compared with siControl transfection (Figure 2C, 2D). Then, colony formation assays were used to analyze the effects of ABHD11-

AS1 knockdown on cell colony formation capabilities. As the data shown in Figure 2E, a decrease in ABHD11-AS1 expression also greatly attenuated the colony-forming ability of both PANC-1 and L3.6pl cells. Moreover, flow cytometric analysis was carried out to further determine the effects of AFAP1-AS1 on the apoptosis of PANC-1 and L3.6pl cells. The data suggested that the knockdown of ABHD11-AS1 increased apoptosis in PANC-1 and L3.6pl cells (Figure 2F). Collectively, our data revealed that ABHD11-AS1 facilitated proliferation and inhibited apoptosis in PC.

Depletion of ABHD11-AS1 Suppressed Cell Metastasis of PC Cells

We next investigated whether ABHD11-AS1 affected the migration and invasion abilities of PC cells. Wound healing assay demonstrated that ABHD11-AS1 knockdown notably decreased the migration ability of PANC-1 cells compared with the control group (Figure 3A). Similarly, the knockdown of ABHD11-AS1 also significantly reduced L3.6pl cells migration (Figure 3B). Furthermore, transwell assay was employed to investigate the effects of ABHD11-AS1 on the invasive ability of PANC-1 and L3.6pl cells *in*

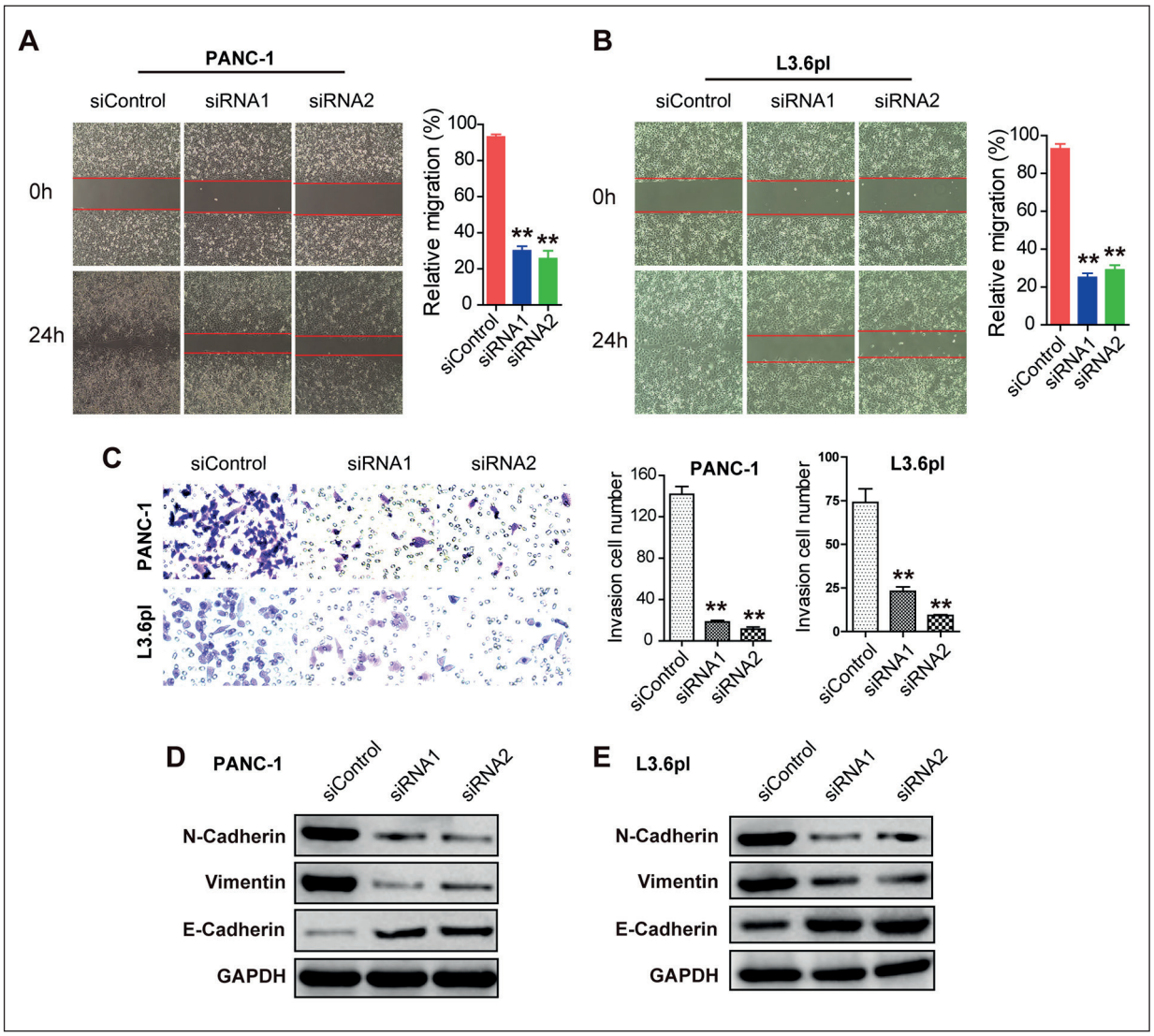

Figure 3. Effects of ABHD11-AS1 knockdown on the migration and invasion of PANC-1 and L3.6pl cells. ***A***, ***B***, Wound healing assay was used to measure the migration capabilities of PANC-1 cells and L3.6pl cell. ***C***, The transwell invasion assay was used to measure the migration abilities of PANC-1 and L3.6pl cells. ***D***, ***E***, The protein expression levels of EMT related molecules were assessed in PANC-1 and L3.6pl cells transfected with siRNA1 or siRNA2 by Western blot analysis. The values were means ± SEM. *$p < 0.05$, **$p < 0.01$.

vitro. According to the data, both PANC-1 and L3.6pl cells transfected siRNA1 or siRNA2 exhibited significant declines in invasion abilities compared with the control group (Figure 3C). In addition, Western blot analysis was performed to determine the expression of EMT related markers such as E-cadherin, N-cadherin and vimentin in PANC-1 and L3.6pl cells. The data revealed that the protein expression levels of both N-cadherin and vimentin were decreased significantly while the epithelial marker E-cadherin was upregulated in PANC-1 and L3.6pl cells transfected with siRNA1 or siRNA2 (Figure 3D, 3E). Our results provided evidence that the knockdown of ABHD11-AS1 could repress migration and invasion of PC cells.

Effects of ABHD11-AS1 Knockdown on PI3K-AKT Signaling in PC Cells

To further explore the potential molecular mechanism by which ABHD11-AS1 affected proliferation, migration and invasion of PC cells, the PI3K-AKT signaling pathway was investigated using Western blot assay. The data confirmed that the protein levels of phosphorylated PI3K (p-PI3K) and phosphorylated AKT (p-AKT) were markedly reduced in PANC-1 cells transfected with siRNA1 and siRNA2 implying that the knockdown of ABHD11-AS1 suppressed the activity of the PI3K-AKT signaling pathway (Figure 4A). Consistent with the data observed in PANC-1 cells, the knockdown of ABHD11-AS1 also significantly reduced the protein levels of both p-PI3K and p-AKT (Figure 4B). Our results demonstrated that ABHD11-AS1 maintained the activity of PI3K-AKT signaling in PC cells.

Discussion

PC patients have a poor outcome. Few of them who undergo curative resection can be alive after

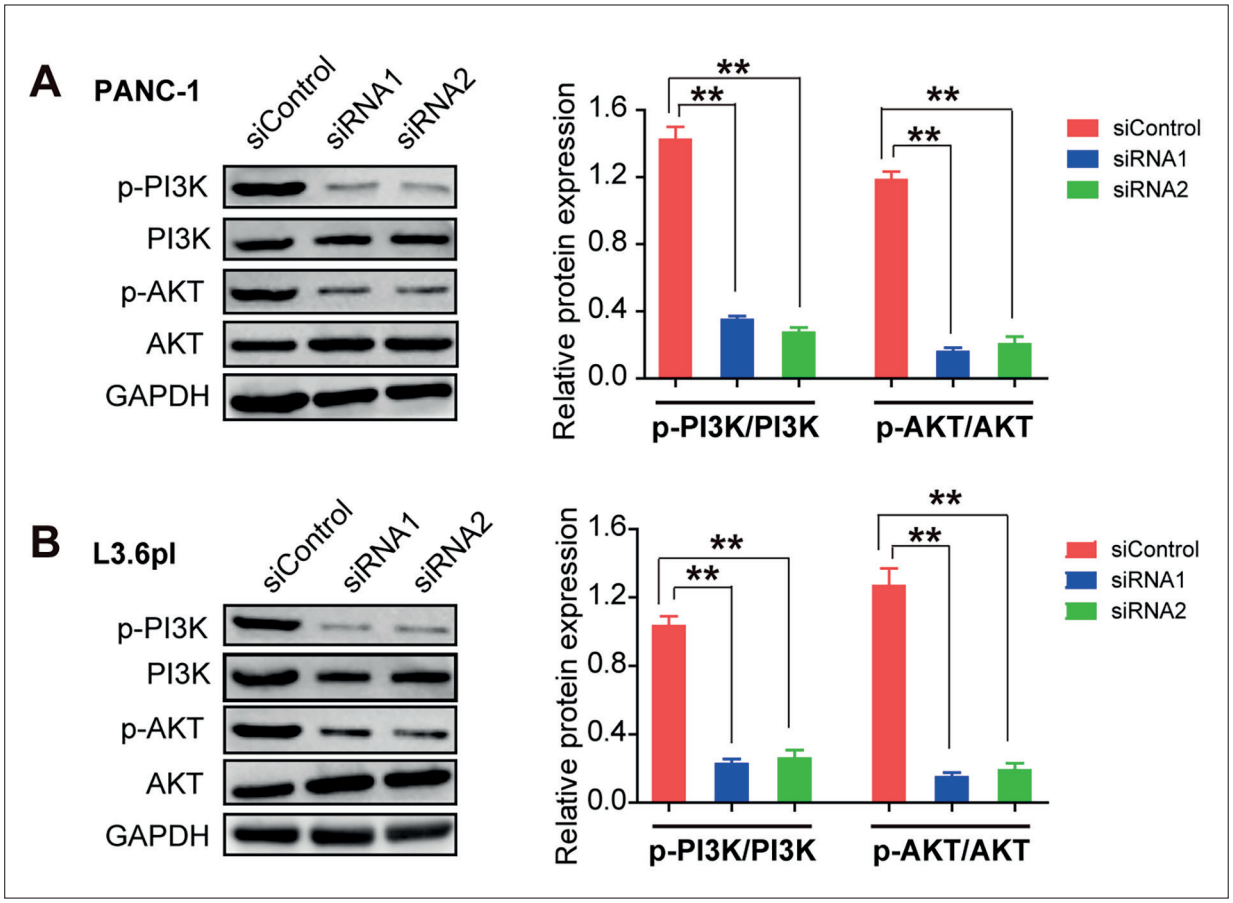

Figure 4. Effects of ABHD11-AS1 on the PI3K/AKT signaling in pancreatic cancer. ***A,*** The protein expression levels of PI3K, p-PI3K, AKT and p-AKT in PANC-1 cells detected by Western blot analysis. ***B,*** The protein expression levels of PI3K, p-PI3K, AKT and p-AKT in L3.6pl cells detected by Western blot analysis. The values were means ± SEM. **p* < 0.05, ***p* < 0.01.

five years[19]. Molecular biomarkers that could be used as prognostic factors would be useful in determining an individualized treatment plan for PC patients[20]. LncRNAs are a new focus because of the benefits of the fast development of sequencing technique and bioinformatics[21]. In this study, we used "GEPIA" which is an online gene expression data to screen differently expressed lncRNA and found that the ABHD11-AS1 expression was significantly up-regulated in PC tissues. In addition, patients with high ABHD11-AS1 had a poorer overall survival and disease-free survival. To further demonstrate previous results, we first detected the expression of ABHD11-AS1 in PC patients by RT-PCR, finding that ABHD11-AS1 expression was significantly up-regulated in PC tissues compared with normal tissues. Subsequent clinical assay indicated that a high level of the ABHD11-AS1 expression was correlated with distant metastasis, TNM stage and tumor differentiation. Moreover, the Kaplan-Meier analysis revealed that high ABHD11-AS1 expression had a significant negative impact on OS. Finally, we confirmed that ABHD11-AS1 expression level was an independent prognostic factor for predicting the 5-year OS of PC patients *via* univariate and multivariate analyses. To our best knowledge, our findings revealed that ABHD11-AS1 could represent a novel biomarker for predicting poor survival of PC patients. Recently, several studies have indicated that the dysregulation of ABHD11-AS1 was involved in the development and progression of various tumors. For instance, gastric juice ABHD11-AS1 was significantly higher expressed in gastric cancer patients and its levels could be used as a potential biomarker in the screening of gastric cancer[14]. ABHD11-AS1 was highly expressed in bladder cancer and positively associated with clinicobiological features, and its knockdown inhibited cell proliferation and migration in bladder cancer, indicating it as a therapeutic target in bladder cancer[15]. LncRNA ABHD11-AS1 played an oncogenic role in endometrial carcinoma by suppressing endometrial carcinoma cells proliferation and invasion by targeting cyclin D1[16]. Another study showed that the expression levels of ABHD11-AS1 were significantly up-regulated in epithelial ovarian cancer. The knockdown of ABHD11-AS1 suppressed epithelial ovarian cancer cell proliferation and metastasis both *in vitro* and *in vivo*, and the inhibitory effects induced by knocking down ABHD11-AS1 mainly depended on the targeted regulation of RhoC[17]. All of the above findings revealed that ABHD11-AS1 was involved in tumorigenesis and it served as a tumor promoter in various tumors. However, the expression and function of ABHD11-AS1 in PC have not been investigated, which prompted us to explore the clinical significance and functions of ABHD11-AS1 in human PC. In this work, we performed a loss-function assay to explore the effect of ABHD11-AS1 on PC cells proliferation, apoptosis and metastasis, finding that ABHD11-AS1 deletion resulted in significant inhibition of cell proliferation, migration, invasion and EMT, while induced apoptosis in PC cells. Our findings suggested ABHD11-AS1 as a tumor promoter in PC. The PI3K/AKT signaling pathway is very important to several physiological and pathological conditions, such as cell proliferation, angiogenesis and survival[22]. In addition, the PI3K/AKT pathway is one of the most important signaling networks in cancer[23-25]. Recently, new evidence indicated that the PI3K/Akt signaling pathway mediates the process of EMT and has attracted widespread attention as a potential therapeutic approach for metastatic tumors[26,27]. To explore the potential molecular mechanism by which ABHD11-AS1 promoted PC proliferation, migration, invasion and EMT, our attention focused on the effect of ABHD11-AS1 on the PI3K/AKT pathway which had been reported to be modulated by several other lncRNAs in various tumors[28-30]. We performed Western blot to detect the expression levels of the PI3K/AKT pathway-related proteins in PC cells transfected with si-ABHD11-AS1 and found that ABHD11-AS1 decreased the level of p-PI3K and p-Akt, but did not significantly decrease PI3K and AKT, suggesting that ABHD11-AS1 may affect PC cells by modulating the PI3K/AKT signaling pathway.

Conclusions

ABHD11-AS1 acts as a tumor promoter gene in PC and can promote cell invasion and migration by activating the PI3K/Akt signaling pathway to promote EMT and PC metastasis. The present findings provide evidence that ABHD11-AS1 may be a prognostic factor and therapeutic target for patients with PC. Our findings enlarge our knowledge in the molecular mechanisms of PC tumorigenesis.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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