

ORIGINAL RESEARCH

FOXD2-AS1 inhibits the proliferation and migration in prostate cancer: an *in vitro* and *in vivo* study

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Abstract

FOXD2 Adjacent Opposite Strand RNA 1 (*FOXD2-AS1*), a long noncoding RNA (lncRNA), exhibits specifically elevated in numerous cancerous cells. Numerous studies have shown that *FOXD2-AS1* encourages cellular proliferation, migration and invasion. Nevertheless, the exact mechanism through which *FOXD2-AS1* contributes to prostate cancer (PCa) remains unclear. Consequently, we aimed to explore the implications of *FOXD2-AS1* on the growth of PCa. Initially, an elevation of *FOXD2-AS1* observed in PCa cells (PC-3, DU145 and Lncap) than the prostate normal cell line RWPE2. Then, PC-3 cells were transfected with sh*FOXD2-AS1*, sh-Numerical Control (shNC) or *FOXD2-AS1* to assess the implications of *FOXD2-AS*. Cell growth was measured with cell counting kit-8 (CCK8) and 5-ethynyl-2'-deoxyuridine (EDU) assays, and cell invasion and migration were assessed by Transwell assays, which demonstrated that *FOXD2-AS1* silence impeded proliferation, migration and invasion of PC-3 cells. Additionally, we discovered that *FOXD2-AS1* bonded with miR-206/programmed cell death protein 10 (*PDCD10*) through analyzing the interaction sites of lncRNA, miRNA and protein. Then, these interaction abilities were confirmed by dual-luciferase reporter assays and RT-qPCR, suggesting *FOXD2-AS1* could upregulate the amount of *PDCD10* through suppressing miR-206. Furthermore, the role of *FOXD2-AS1* silencing on PCa carcinogenesis were assessed. *In vivo* experiment, sh*FOXD2-AS1* led to a notable reduction in both the size and weight of PCa. These findings indicated that *FOXD2-AS1* silencing effectively hindered the progression of prostate cancer. In conclusion, the upregulation of *FOXD2-AS1* was observed in PCa, and the knockdown of *FOXD2-AS1* could alleviate tumor development by targeting miR-206 to upregulate *PDCD10* expression.

Keywords

FOXD2-AS1; Prostate cancer; miR-206; PDCD10

1. Introduction

1.1 What is known?

- The lncRNA-miRNA-mRNA axis is considered the most common molecular mechanism in tumor pathogenesis, influencing tumor pathogenesis at the transcription level.

- However, there have been limited investigations into the involvement of the lncRNA-miRNA-mRNA pathway in prostate cancer.

1.2 What new results were revealed?

- *FOXD2-AS1* is elevated in prostate cancer than normal cells.

- Downregulation of *FOXD2-AS1* suppressed tumor growth and metastasis in both *in vitro* and *in vivo*.

- We highlight the effect of the *FOXD2-AS1*-miR-206-*PDCD10* pathway in prostate tumor genesis.

- The current study addresses a significant and increasing

clinical problem by targeting *FOXD2-AS1* knocked out to alleviate prostate cancer progression. Additionally, *FOXD2-AS1* could act as a novel biomarker for determining the advancement of prostate cancer.

Prostate cancer (PCa) stands as one of the most prevalent malignancies and remains a primary contributor to cancer-associated mortality in men [1]. Initial treatment for PCa typically involves androgen ablation, which effectively suppresses tumor regression in the early stages [2]. However, as PCa advances, the androgen receptor (AR) often becomes constitutively active even when devoid of androgens [3]. To effectively address and manage aggressive and metastatic forms of the disease, identifying biomarkers capable of predicting clinical progression and guiding treatment approaches is of paramount importance. In various tumor types [4], including prostate cancer, aberrations in the activity of tumor-associated genes play a significant role in driving tumor growth.

Long noncoding RNAs (lncRNAs), comprising RNA

molecules exceeding 200 nucleotides in length and devoid of protein-coding potential, are progressively acknowledged as central participants in a variety of cellular mechanisms and biological activities. They exert their effects through various mechanisms, including epigenetic modifications, microRNA (miRNA) modulation and mRNA stability. Notably, lncRNAs play a significant regulatory role in PCa by sequestering miRNAs [5, 6]. For instance, the silencing lncRNA Nuclear Enriched Abundant Transcript 1 (*NEAT1*) promotes miR-776-5p expression, hence suppressing the proto-oncogene E2F transcription factor 3 (*E2F3*), which in turn reduces cell proliferation, invasiveness and migration of prostate cancer [7]. *MALAT1* exerts a suppressive effect on the malignant phenotype of PCa via the modulation of miR-423-5p [7, 8]. *oIP5-AS1* functions as a miR-128-3p sponge, leading to increase the light chain subunit solute carrier family 7 member 11 (*SLC7A11*), which subsequently inhibits ferroptosis and facilitates cancer progression in PCa [9]. *FOXD2-AS1* emerges as a critical regulator in tumorigenesis. Studies have demonstrated that dysregulated *FOXD2-AS1* renders gastric cancer cells more sensitive to radiation through modulation of the *miR-1913/SET* binding protein 1 (*SETD1A*) axis [10]. Suppression of *FOXD2-AS1* attenuates cell proliferation, while its upregulation increased *miR-31* expression and consequent dysregulation of Paired box 9 (*PAX9*) expression in retinoblastoma [11]. Additionally, *FOXD2-AS1* contributes to the advancement of papillary thyroid cancer through its modulation of the *miR-485-5p/kallikrein-related peptidase 7 (KLK7)* [12]. However, the involvement of *FOXD2-AS1* in PCa has been less extensively studied, and its underlying mechanisms remain unclear.

It has been found that *FOXD2-AS1* can bind miR-206 and inhibit its expression [13]. Utilizing Starbase online prediction tool has suggested a potential binding interaction between miR-206 and *PDCD10*. Extensive research has demonstrated that the downregulation of *PDCD10* inhibits PCa proliferation and migration [14, 15]. Therefore, we hypothesize that the interaction between *FOXD2-AS1*, miR-206 and *PDCD10* might hold substantial importance in the context of prostate cancer.

Here, we discovered that suppressing *FOXD2-AS1* could inhibit the growth and migration of PCa cells by a mechanism connected to the control of the *miR-206/PDCD10*. Additionally, *FOXD2-AS1* suppression reduced tumor progression in an *in vivo* model.

2. Methods

2.1 Cell culture and transfection

Normal prostate cell line RWPE1 (CRL-2854) and the human PCa cell lines PC-3 (CRL-1435), DU145 (HTB-81) and Lncap (CRL-1740) were acquired from the American Type Culture Collection (ATCC). The cells were grown in a controlled incubator setting (5% carbon dioxide (CO₂), 37 °C) using Dulbecco's Modified Eagle's Medium (DMEM) (111965092, Gibco, Waltham, MA, USA) as the culture medium, along with 10% fetal bovine serum (FBS, 26140079, Gibco, Waltham, MA, USA) and 1% penicillin/streptomycin supplementation.

After 12 hours of incubation in a 12-well plate, 2×10^5 cells

were subjected to transfection with *FOXD2-AS1*, sh*FOXD2-AS1* and shRNA-negative control (shNC) using Lipofectamine 2000 reagent (0.5 μL, Invitrogen).

2.2 Animals

A group of twelve BALB/c nude mice, aged between 6 and 8 weeks, were kept in a standard housing condition for 7 days prior to the commencement of the experiments. Subsequently, they were divided into two separate groups through random selection: shNC group (n = 6) and sh*FOXD2-AS1* group (n = 6). A xenograft tumor model was created involved the subcutaneous injection of 5×10^6 PCa cells.

2.3 Real-time quantitative polymerase chain reaction (RT-qPCR)

Total RNA was extracted using TRIzol, and its concentration was determined using a spectrophotometer (912A0973-1Y, Thermo Fisher Scientific, Inc., Waltham, MA, USA). Subsequently, the reverse transcription process was carried out using the Transcriptor cDNA Synthesis Kit (04379012001, Roche, Boston, MA, USA) to convert RNA into cDNA. The primer sequences used for the amplification of specific targets were as follows: forward: 5'-CTCACATCCGGCGGCT-3', reverse: 5'-GGCTGTTCATGATATGTGCCA-3'; miR-206 primer: forward: 5'-TAAGGCACCCTTCTGAGTAGA-3', reverse: 5'-GCGAGCACAGAATTAATACGAC-3'; *PDCD10* primer: forward: 5'-CAGACACTGAGAGCCGCTTTCA-3', reverse: 5'-CTGCCATACGAAGAAGGGACTC-3'.

2.4 Cell proliferation and viability

Viability and proliferation were evaluated through CCK8 and EDU assays. For the CCK8 assay, PCa cells (2×10^5 cells) were plated in 96-well plates. After 24 hours, 10 μL of CCK8 solution was introduced to each well and left for 4 hours. Cell viability was evaluated by measuring the optical density (OD) at 450 nm. For the EDU, PCa cells were quantified and then placed onto 96-well plates. After that, cells were made permeable with 0.3% Triton X-100 and then fixed using 4% paraformaldehyde. They were then exposed to a reaction solution in the dark at 37 °C for 30 minutes. Following this, nuclei staining of the cells took place. Cell proliferation activity was assessed by measuring EDU-stained cells.

2.5 Flow cytometry

The eBioscience Apoptosis Detection Kit (88-8005-72) was employed for detecting apoptotic cells. PCa cells (3×10^5 /well) were plated in 6-well plates and cultured for 24 hours. Afterward, the cells underwent a Phosphate-buffered saline (PBS) wash and then subjected to a 15-minute incubation with Annexin V-FITC. The cells suspension received an addition of Propidium iodide (PI) before being analysed via a FACS-Calibur flow cytometer (643438, Becton Dickinson, Franklin Lakes, NJ, USA).

2.6 Transwell assay

To assess cell migration and invasion in PCa cells, the Transwell test was performed. Briefly, DMEM medium mixed with diluted Matrigel gel (Corning, USA, 356234) was evenly dispensed onto the upper chamber of Transwell inserts (Boyden chambers, neuroprobe, BY312) and incubated at 37 °C to allow gel solidification. Subsequently, a total of 3×10^5 PCa cells were placed into the upper compartment, while the lower compartment was supplied with culture media enriched with FBS. After incubating for 24 hours to migration and invasion, the cells situated on upper were removed. Meanwhile, cells that had migrated or invaded through the membrane were immobilized using 4% paraformaldehyde (Xuanya, XY-PCR-1654) and then stained by 1% crystal violet (Beyotime, China). Finally, five random visual perspectives were chosen from each group, and images were captured using a microscope.

2.7 Wound healing assay

PCa cells (3×10^5 cells) were placed and grown until they formed 80%–90% confluence. After treatments, cells were deprived of nutrients overnight using a medium containing 1% FBS (26140079, Gibco, Waltham, MA, USA). Then, a linear scratch was generated by gently scraping the fully grown cell layer using a 200 μ L pipette tip. After rinsing, the cells were cultured with complete medium for 24 hours. Images of the scratches were captured using a phase contrast microscope.

2.8 Western blot assay

Cell lysis used RIPA buffer (P0013C, Beyotime, Shanghai, China), followed by protein debris removal through centrifugation. Protein concentration was determined using the BCA kit (P0009, Beyotime, Shanghai, China). Proteins were electrophoresed based on molecular weights, then transferred to polyvinylidene fluoride (PVDF) membranes and exposed to 5% non-fat dry milk at room temperature for 1 hour. After Tris-buffered saline with 0.1% Tween® 20 detergent (TBST) rinsing, membranes were incubated overnight at 4 °C with primary antibodies. Secondary antibodies were applied post primary exposure and incubated at 37 °C for 1 hour. Electrochemiluminescence (ECL) detection (GE Healthcare, Piscataway, NJ, USA) visualized protein bands. Primary antibodies: E-cadherin (#ab40772), Vimentin (#ab92547), α -SMA (#ab5831), β -actin (#ab8226) from Abcam. Secondary antibodies: anti-mouse (#4410, 1:10000), anti-rabbit (#4414, 1:10000) from Cell Signaling Technologies.

2.9 Luciferase activity

Invitrogen (Thermo Fisher Scientific, USA) synthesized the sequences of FOXD2-AS1 or PDCD10. Two versions of these sequences were generated, one with the anticipated binding sites for miR-206 (designated as WT) and the other lacking these binding sites (designated as MUT). PCa cells were co-transfected with a reporter vector containing these sequences and either a miR-206 mimic or a negative control (NC) mimic. The luciferase activities of these cells were measured using the dual-luciferase assay (Promega, USA).

2.10 In vivo experiment

Four-week-old BALB/c nude mice were randomized into two groups (shNC and shFOXD2-AS1), each comprising six animals. The mice were then subcutaneously injected with 5×10^6 PCa cells that had been transfected with either shNC or shFOXD2-AS1. The tumor volume and weight were measured at specific time points (8, 10, 12, 14, 16, 18 and 20 days) after the injection. The tumor volume was calculated using the formula: $1/2 \times (\text{length}) \times (\text{width})^2$.

2.11 Immunohistochemistry

Tumor tissue sections were fixed in 4% paraformaldehyde (PFA) for 2 hours, washed with PBS, then incubated with 2% bovine serum albumin (BSA) and 0.5% Triton X-100 for 1 hour at 25 °C, followed by cultivating with primary antibodies for 2 hours. After washing with PBS and cultured with secondary antibodies for an hour, the tissue sections were stained with Ki67 (1:1000) for 5 minutes. The immunofluorescence staining was captured and visualized using a confocal microscope (Nikon, Tokyo, Japan).

2.12 Statistical analysis

The data were statistically analyzed using SPSS 22.0 (IBM, Armonk, NY, USA). Significance between different groups was assessed using the student *t*-test and analysis of variance (ANOVA) analysis. The results from three separate experiments are presented as means with their corresponding standard deviations (SD). A *p*-value < 0.05 is considered statistically significant.

3. Results

3.1 FOXD2-AS1 knockdown inhibits the proliferation of PCa cells

We initially performed RT-qPCR to identify FOXD2-AS1 levels in the normal prostate cell line RWPE2 and the PCa cell lines, namely PC-3, DU145 and Lncap, to assess the levels of FOXD2-AS1 expression and its impact on the biological characteristics of prostate cancer. The levels of FOXD2-AS1 were substantially higher in PC-3, DU145 and Lncap cells compared to RWPE2 cells (Fig. 1A). Then, PCa cells were transfected using shFOXD2-AS1, shNC or FOXD2-AS1 to determine the impact of FOXD2-AS1 on tumorigenesis. The shFOXD2-AS1 group exhibited a noteworthy decrease in the expression of FOXD2-AS1, while the FOXD2-AS1 overexpressed group showed a marked elevation in FOXD2-AS1 expression (Fig. 1B). Subsequently, we explored the impact of FOXD2-AS1 on cell viability through CCK8 assays (Fig. 1C), EDU assays (Fig. 1D) and flow cytometry (Fig. 1E). The results showed a significant increase in both the optical density (OD) value (Fig. 1C) and the count of proliferating cells (Fig. 1D) in the FOXD2-AS1 overexpressed cells, while those of the sh-FOXD2-AS1 group showed opposite results. Moreover, shFOXD2-AS1 transfection resulted in a notable rise in apoptosis rates of PCa cells (Fig. 1E). Collectively, these results indicate the substantial restraining impact of FOXD2-AS1 suppression on PCa growth and metastasis while promot-

ing cell apoptosis.

3.2 FOXD2-AS1 knockdown repressed the migration of PCa cells

Here, we investigated how FOXD2-AS1 impacts PCa cell metastasis using Transwell assay. Compared to the shNC group, cells transfected with shFOXD2-AS1 exhibited a reduced number of migrated cells (Fig. 2A). Similarly, the invasion of PCa cells was substantially decreased upon silenced FOXD2-AS1 (Fig. 2B). Next, a western blot analysis was conducted to evaluate how FOXD2-AS1 impacts the expression of epithelial-mesenchymal transition (EMT) markers in PCa cells. Silencing FOXD2-AS1 resulted in a substantial rise in the levels of the epithelial marker (E-cadherin), coupled with a reduction in the mesenchymal markers (Vimentin and α -smooth muscle actin (α -SMA)) compared to the control (Fig. 2C). These findings provide evidence that FOXD2-AS1 silencing suppressed the migration and invasion of PCa cells.

3.3 FOXD2-AS1 deregulates the expression of miR-206

Our investigation revealed a potential interaction between FOXD2-AS1 and miR-206, which could affect cell proliferation, migration and invasion. We assessed the binding sites between FOXD2-AS1 and miR-206 (Fig. 3A). Notably, PCa cells transfected with FOXD2-AS1 exhibited significantly reduced levels of miR-206 expression compared to control cells (Fig. 3B). To further validate this interaction, we carried out a luciferase reporter test. The data demonstrated that the significant decrease in luciferase activity was observed in cells containing FOXD2-AS1 when miR-206 was overexpressed, as opposed to FOXD2-AS1-MUT cells (Fig. 3C). These data support the relationship between FOXD2-AS1 and miR-206, which implies that FOXD2-AS1 may inhibit miR-206.

3.4 miR-206 targets the expression of PDCD10

We then predicted potential targets of miR-206 and focused on PDCD10 based on previous studies. The interaction sites involving miR-206 and PDCD10 can be observed in Fig. 4A.

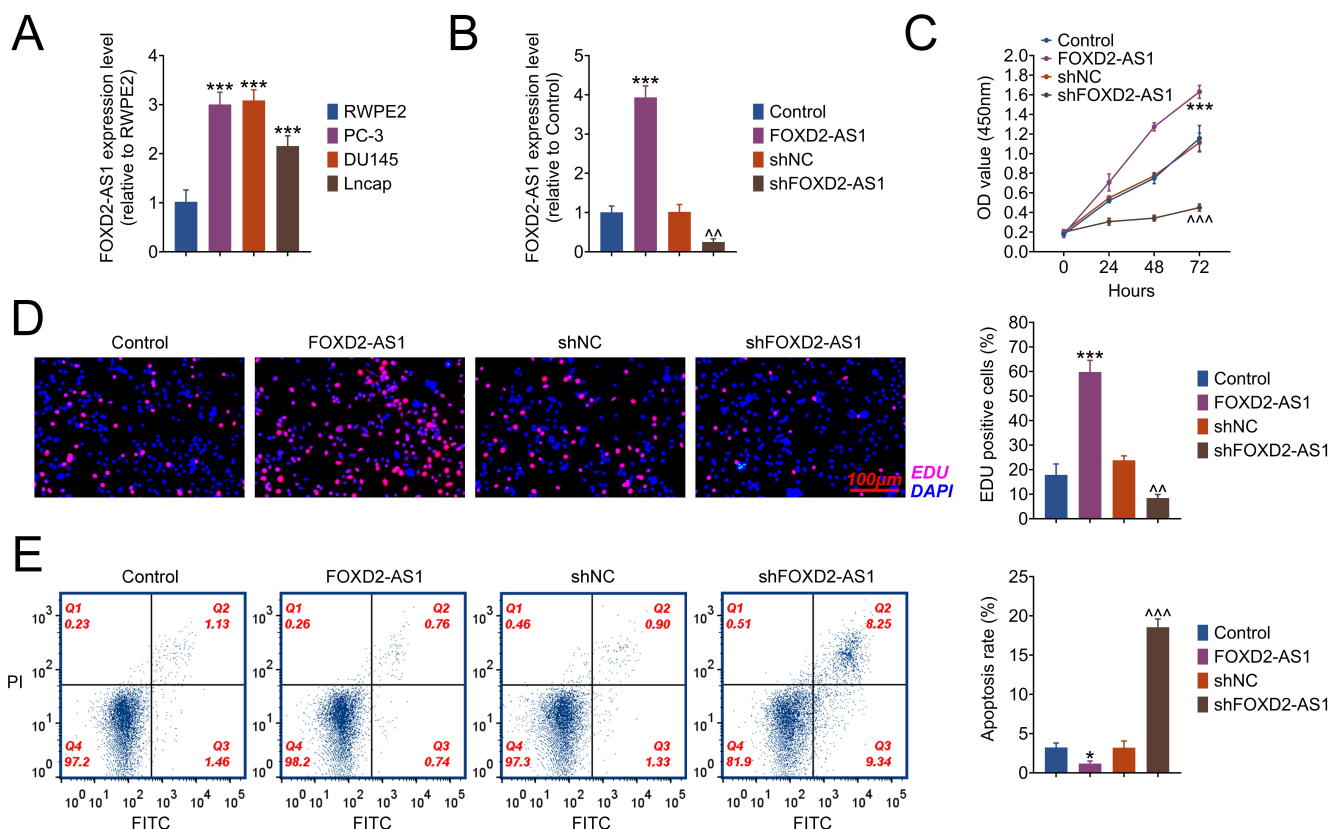


FIGURE 1. FOXD2-AS1 knockdown inhibits the proliferation of prostate cancer cells. (A) The levels of FOXD2-AS1 were measured in both normal prostate cell (RWPE2) and PCa cell lines (PC-3, DU145 and Lncap) using RT-qPCR. *** $p < 0.001$ vs. RWPE2 cells. (B) FOXD2-AS1 was determined by RT-qPCR in PCa cells transfected with shFOXD2-AS1, shNC or FOXD2-AS1. (C) The cell availability (shown in OD value) was assessed in PCa cells by CCK8. (D) The ability of proliferation was evaluated by EDU assays using PCa cells. (E) The apoptosis rate of PCa cells was measured by flow cytometry. The data are expressed as the mean \pm SD. * $p < 0.5$, *** $p < 0.001$ vs. control. ^ $p < 0.01$, ^^ $p < 0.001$ vs. FOXD2-AS1 group. FOXD2-AS1: FOXD2 Adjacent Opposite Strand RNA 1; shNC: sh-Numerical Control; OD: optical density; EDU: 5-ethynyl-2'-deoxyuridine; DAPI: 4',6-diamidino-2-phenylindole; PI: propidium iodide; FITC: fluorescein isothiocyanate.

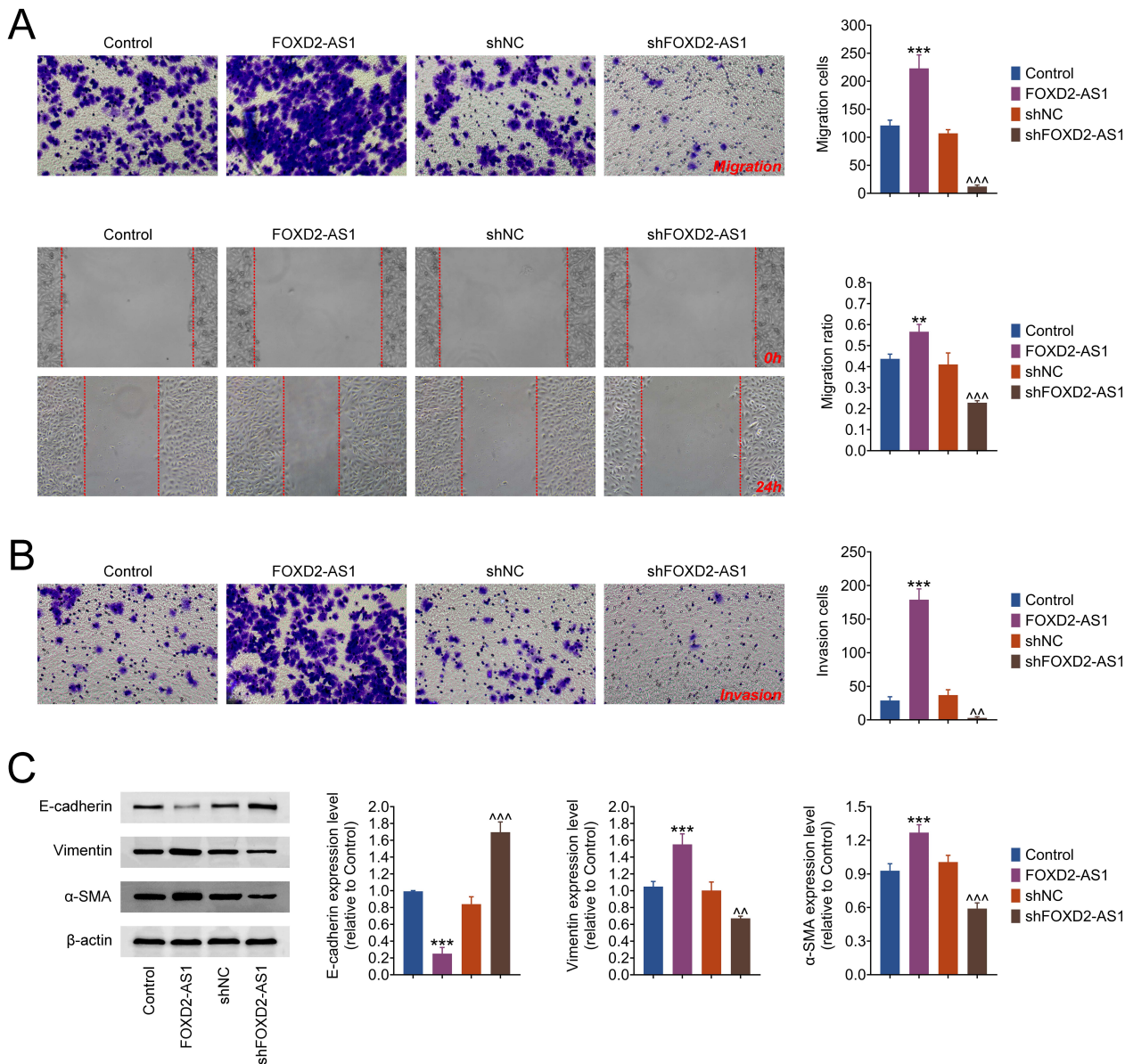


FIGURE 2. FOXD2-AS1 silencing repressed the migration of prostate cancer cells. (A) The migration was assessed by Transwell assay. (B) The invasion was detected by Transwell and wound healing. (C) The levels of E-cadherin, Vimentin and α -SMA were measured by western blot, normalized to β -actin. The data are expressed as the mean \pm SD. *** $p < 0.001$ vs. control. ^^ $p < 0.01$, ^^ $p < 0.001$ vs. FOXD2-AS1 group, ** $p < 0.01$. FOXD2-AS1: FOXD2 Adjacent Opposite Strand RNA 1; shNC: sh-Numerical Control; α -SMA: α -smooth muscle actin.

We used RT-qPCR and western blot analysis to assess PDCD10 levels in PCa cells, revealing miR-206's suppressive effect on PDCD10 expression (Fig. 4B), where miR-206 overexpression significantly decreased luciferase activities in PDCD10-WT cells but not in PDCD10-MUT cells (Fig. 4C). Furthermore, we investigated FOXD2-AS1's impact on PDCD10 expression. qPCR analysis showed increased PDCD10 expression upon FOXD2-AS1 overexpression, which was counteracted by miR-206 overexpression (Fig. 4D). These findings demonstrate that FOXD2-AS1 increased PDCD10 levels by suppressing miR-206 activity.

3.5 FOXD2-AS1 knockdown suppressed the development of PCa *in vivo*

PCa cells were transfected with either shNC or shFOX2-AS1 and then administered subcutaneously to mice to assess tumor size and weight and provide robust evidence of FOXD2-AS1's activity (Fig. 5A). Our results showed a noteworthy decrease in both tumor volume (Fig. 5B) and weight (Fig. 5C) in the shFOX2-AS1-treated PCa cells compared to those treated with shNC. Additionally, we conducted immunohistochemistry to assess the growth capacity of cells within tumor tissues, and the results revealed a notable reduction in Ki67 expression in tissues treated with shFOX2-AS1 compared to those treated with shNC (Fig. 5D), indicating that shFOX2-AS1 silencing could suppress the tumor progression *in vivo*.

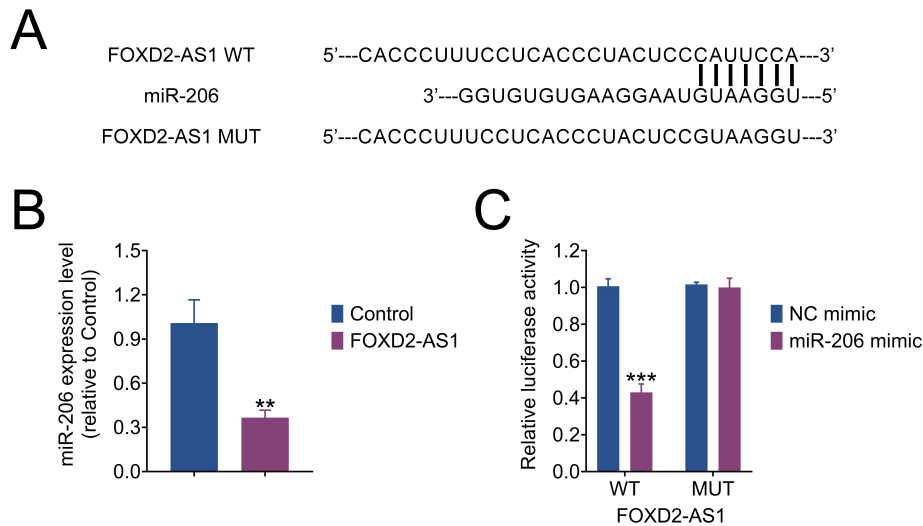


FIGURE 3. FOXD2-AS1 deregulates the expression of miR-206. (A) Binding sites in FOXD2-AS1 versus miR-206. (B) miR-206 expression in PCa cells with FOXD2-AS1 detected by RT-qPCR. (C) Binding sites in PCa cells were investigated by dual-luciferase assays. The results are expressed as the mean \pm SD. $**p < 0.01$, $***p < 0.001$ vs. control or NC mimic. FOXD2-AS1: FOXD2 Adjacent Opposite Strand RNA 1; WT: wild type; MUT: mutation; NC: Numerical Control.

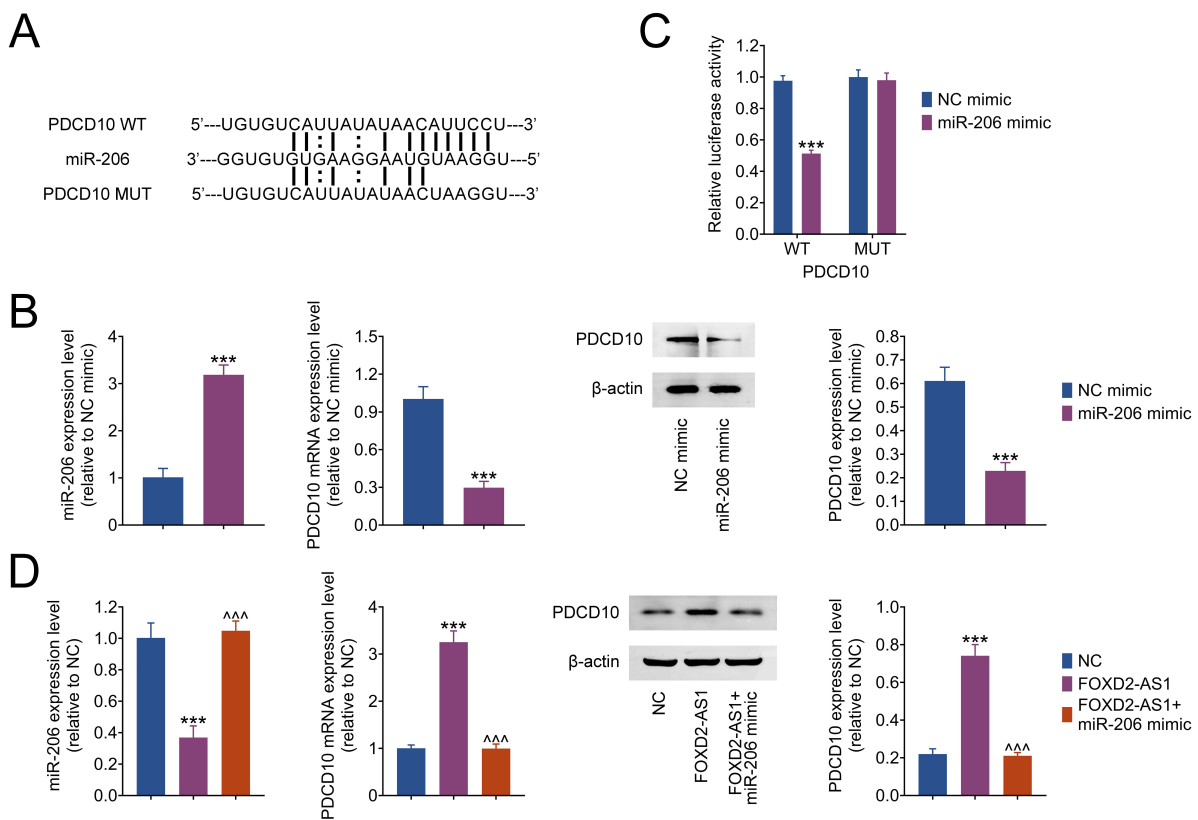


FIGURE 4. miR-206 targets the expression of PDCD10. (A) MiR-206 binding sites within PDCD10. (B) miR-206 mimic effects on PDCD10 in PCa cells was evaluated by RT-qPCR and western blot. (C) Associations of miR-206 with the PDCD10 in PCa cells were shown by dual-luciferase assay. (D) RT-qPCR and western blot show that FOXD2-AS1 raised PDCD10 levels by inhibiting miR-206. The results are expressed as the mean \pm SD. $***p < 0.001$ vs. NC mimic. $^^^p < 0.001$ vs. FOXD2-AS1 group. FOXD2-AS1: FOXD2 Adjacent Opposite Strand RNA 1; PDCD10: programmed cell death protein 10; WT: wild type; MUT: mutation; NC: Numerical Control.

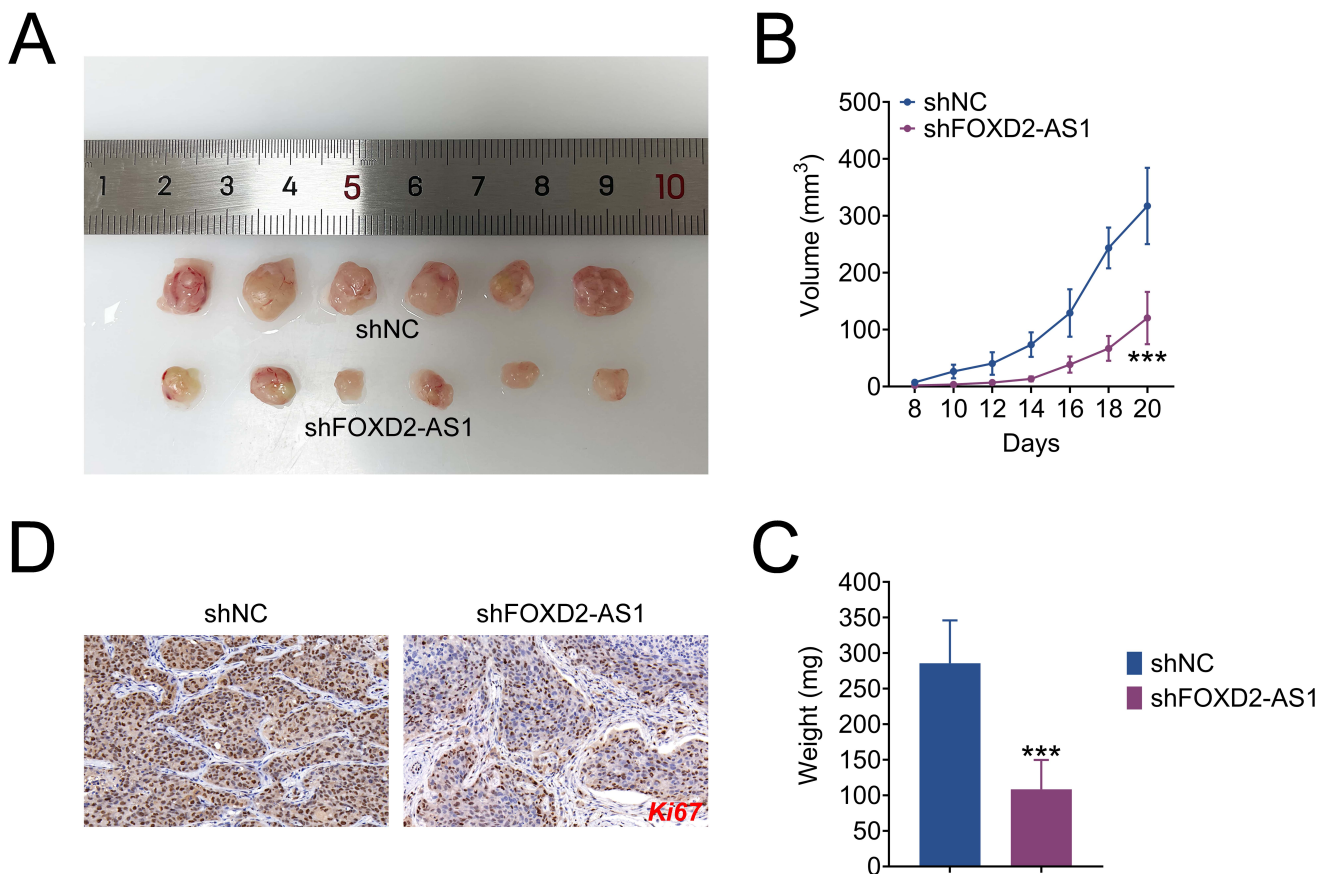


FIGURE 5. FOXD2-AS1 silencing suppressed the development of prostate cancer *in vivo*. (A) The picture of tumor tissues in each group. (B) The size of the tumor in nude mice that received injections of PCa cells transfected with shNC and shFOXD2-AS1. (C) The tumor weight was observed in nude mice that were injected with PCa cells transfected with both shNC and shFOXD2-AS1. (D) The proliferation (shown in Ki67) of tumors was analyzed by immunohistochemistry. The results are expressed as the mean \pm SD. *** $p < 0.001$ vs. shNC. FOXD2-AS1: FOXD2 Adjacent Opposite Strand RNA 1. ShNC: sh-Numerical Control.

4. Discussion

Despite ongoing efforts, the underlying molecular basis of PCa remains elusive, leading to its increasing prevalence and fatality each year. In this research, we observed that FOXD2-AS1 level was dramatically increased in PCa cells in comparison to normal prostate cells. Importantly, FOXD2-AS1 suppression reduced tumor growth, migration and invasion of PCa cells *in vitro*, which was further validated in an *in vivo* model, where FOXD2-AS1 silencing reduced PCa progression. Moreover, our investigation highlighted the pivotal role of FOXD2-AS1 in modulating the miR-206/PDCD10 axis. Collectively, these findings provide compelling evidence that the knockdown of FOXD2-AS1 holds promise as a potent strategy to effectively counteract PCa development.

Numerous studies have described the crucial roles of lncRNAs in regulating tumorigenesis. FOXD2-AS1, a member of the lncRNA family, holds significant biological relevance in prostate cancer. Our investigation revealed pronounced suppression of proliferation and migration in FOXD2-AS1 knock-down PCa cells than shNC. To explore the impact of FOXD2-AS1 on PCa biology, we investigated its potential interaction

with miR-206. Predictive analysis revealed a plausible binding association between FOXD2-AS1 and miR-206. To uncover the underlying molecular mechanism, luciferase reporter gene assays were performed. RT-qPCR analysis demonstrated the ability of FOXD2-AS1 to negatively regulate miR-206 expression.

Moreover, miRNAs directly associate with an array of target genes, thereby intricately impacting tumor progression and development. In our investigation, predictive analysis unveiled a possible interaction between miR-206 and the three prime untranslated region (3'-UTR) of the PDCD10 gene. PDCD10 assumes a pivotal role as a significant gene linked to tumor development across various malignancies. Notably, escalated PDCD10 expression has been observed in osteosarcoma, contributing to tumor proliferation, migration and invasion [16]. Similarly, prior studies have suggested that PDCD10, a target of miR-206, can effectively restrain the proliferation of PCa cells [15]. Our study also revealed that PDCD10 was inversely linked with that of miR-206 and associated with FOXD2-AS1 expression, indicating that FOXD2-AS1 may influence tumorigenesis by modulating the miR-206/PDCD10 axis.

To comprehensively assess the effect of FOXD2-AS1 on

in vivo tumor development, we implanted shFOXD2-AS1-transfected PCa cells into mice subcutaneously and measured the viability of the tumors. The data confirmed that shFOXD2-AS1 inhibited both volume and weight in prostate cancer.

In conclusion, the findings demonstrate a significantly high expression of FOXD2-AS1 in PCa cells and that FOXD2-AS1 knockdown inhibited the tumor proliferation and metastasis in both *vitro* and *vivo*, indicating the potential consideration to target FOXD2-AS1 for attenuating the advancement of PCa through the miR-206/PDCD10 axis.

5. Conclusions

The expression of FOXD2-AS1 was found to be elevated in PCa cells and suppression of FOXD2-AS1 led to a reduction in tumor growth by interacting with miR-206 to enhance the expression of PDCD10.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

XM—designed the study and carried them out; XM, YLN and JC—supervised the data collection, analyzed the data, interpreted the data; XM and WW—prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This process received the endorsement of the Ethics Committee of Sinopharm Han Jiang Hospital.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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