Am J Transl Res 2025;17(8):5962-5974
www.ajtr.org /ISSN:1943-8141/AJTR0163272

Original Article

FBXO22 regulates proliferation, migration, and invasion of esophageal cancer cells via the WNT/β-catenin signaling pathway

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Received January 12, 2025; Accepted July 8, 2025; Epub August 15, 2025; Published August 30, 2025

Abstract: Objectives: FBXO22, a member of the F-box family, plays a crucial role in cancer development and progression. However, its expression and biological functions in esophageal cancer (ESCA) remain poorly understood. Methods: In this study, we investigated FBXO22 expression in ESCA cancer tissues using immunohistochemistry and Western blot analyses. Functional assays, including CCK-8, flow cytometry, Western blot, scratch healing, and Transwell migration and invasion assays, were employed to evaluate the effects of FBXO22 modulation on ESCA cell viability, apoptosis, migration, and invasion. Additionally, a nude mouse model was used to assess the impact of FBXO22 silencing on tumor growth. Results: We found that FBXO22 expression was upregulated in ESCA tissues compared to normal tissues. Silencing FBXO22 inhibited ESCA cell viability, migration and invasion while promoting apoptosis. Conversely, FBXO22 overexpression had the opposite effects. Mechanistically, FBXO22 was found to influence the WNT/β-catenin signaling pathway, and its silencing retarded tumor growth in vivo. Conclusions: Our findings highlight the critical role of FBXO22 in ESCA progression and suggest it as a potential therapeutic target for ESCA.

Keywords: FBXO22, Wnt, β-catenin, ESCC, tumorigenesis

Introduction

Esophageal cancer (ESCA) encompasses malignant tumors, primarily esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC) [1]. ESCA is one of the most common malignancies worldwide [2]. Early-stage esophageal cancer is typically asymptomatic, leading to a high propensity for metastasis and invasion, with a five-year survival rate of less than 25%. With over 400,000 deaths annually, ESCA ranks as the sixth leading cause of cancer-related mortality worldwide [3-5]. Current treatments include surgical resection, endoscopic procedures, chemoradiotherapy, and drug therapy; however, surgical interventions are often accompanied by significant complications [6]. Despite advancements in medical technologies, the mortality rate of ESCA remains alarmingly high. This is attributed to the absence of obvious early symptoms and insufficient diagnostic methods, as well as the tumor's characteristics of distal metastasis and local recurrence [7, 8]. Therefore, there is a pressing need to unravel the molecular basis underlying esophageal tumorigenesis and identify more effective therapeutic strategies.

F-box proteins have been revealed to influence tumorigenesis and progression in various can-

https://doi.org/10.62347/TOAI4814

cer types [9-11]. FBXO22, a member of the F-box protein family, contains a 40-amino-acid F-box domain. It binds to Skp-1 and interacts with Cullin-1 to form the SCF (Skp-1, Cullin-1, F-box protein) complex, a critical component of ubiquitin E3 ligases [12]. Research suggests that FBXO22 may be associated with stroke and neurodegenerative diseases [13]. Additionally, FBXO22, p53, and KDM4A can form a ternary complex involved in regulating cellular senescence [14, 15]. FBXO22 has also been implicated in cancer progression. For example, FBXO22 can target and degrade the tumor suppressor Krüppel-like factor 4 (KLF4), promoting hepatocellular carcinogenesis [16]. Elevated FBXO22 expression has been observed in various malignancies, including lung cancer, cervical cancer, and melanoma [17-23]. However, the role of FBXO22 in esophageal carcinogenesis and progression has not yet been elucidated.

In this study, we investigated the expression level of FBXO22 in ESCA tissues and explored its effects on the function of ESCA cells, along with the underlying mechanisms. Our aim was to elucidate the role of FBXO22 in ESCA cells to provide novel insights for the clinical treatment of this malignancy.

Materials and methods

Tissue samples

Tissue microarrays (TMAs) were purchased from Shanghai Xinchao Biotechnology Company (Shanghai, China). Additionally, 10 ESCA tissues and their corresponding paraneoplastic tissues were collected from the First Affiliated Hospital of Bengbu Medical University between October 2022 and December 2022. The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Bengbu Medical University.

Cell lines and culture

Human ESCA cell lines (EC9076 and KYSE150) were purchased from the Cell Bank of the Chinese Academy of Sciences (Shanghai, China). The human esophageal carcinoma cell line TE-1 and human normal esophageal epithelial cells (HEEC) were obtained from Elabscience (Wuhan, China). All cell lines were cultured in RPMI-1640 medium (Gibco, USA) supplemented with 10% inactivated fetal bovine serum (FBS, Evergeen, China) and 1% penicillin-streptomycin. The cells were maintained in an incubator at 37°C with 5% CO_2.

Transfection

The plasmid pCDNA-FBXO22 and the control pCDNA plasmids were purchased from Wuhan U-Bio (Wuhan, China). FBXO22 and β-catenin-specific small interfering RNAs (siRNAs) were synthesized by General Biol (Hefei, China). The siRNA sequence for FBXO22 is 5'-CCUCAAAG-CGGGCCAACAUUTT-3'. The siRNA sequence for β-catenin is 5'-GGGUUCAGAUGAUAUAAAUTT-3'. ESCA cells were seeded in six-well plates and transfected using Lip8000™ transfection reagent (Beyotime, Shanghai, China) following the manufacturer's protocol.

CCK-8 assay

EC9706 and KYSE150 cells (5×10^3) were seeded in 96-well plates. After overnight incubation, the cells were transfected with FBXO22 cDNA or FBXO22 siRNA for 72 hours. Following this, the medium was aspirated, and 100 μl of fresh medium was added to each well, along with 10 μl of CCK-8 reagent (Biosharp, Nanjing, China). After incubation for 1-4 hours, absorbance values were measured at 450 nm using a microplate reader.

RT-PCR

Total RNA was isolated from ESCA cells using Trizol reagent (Biosharp, Nanjing, China) and complementary DNA (cDNA) was synthesized using a reverse transcription kit (Beyotime, Shanghai, China). Quantitative real-time PCR (qRT-PCR) was performed using the SYBR Green PCR Mix kit (Biosharp, Nanjing, China) to measure FBXO22 mRNA expression. The following primer sequences were used: FBXO22: Forward, 5'-ATT GCT GTA AGG TGG GAG CC-3'; Reverse, 5'-ACC CCA AAG TGA CAA AAC CTG-3'. GAPDH: Forward, 5'-GAA AGC CTG CCG GTG ACT AA-3'; Reverse, 5'-GCC CAA TAC GAC CAA ATC AGA G-3'.

Apoptosis analysis

An Annexin V-FITC/PI Apoptosis Assay Kit was purchased from Unitech Bioscience Company (Hangzhou, China) for apoptosis detection.

Briefly, after 48 hours of transfection, ESCA cells were harvested and resuspended in 500 µl of 1× binding buffer at a density of 1 × 10^6 cells/ml. The suspension was incubated with 5 µl of Annexin V-FITC and 10 µl of PI at room temperature in the dark for 5 minutes. Apoptotic cells were analyzed using flow cytometry (Beckman Coulter, USA).

Wound healing assays

Transfected ESCA cells were cultured in six-well plates until they reached 90% confluence. A sterile 100 µl pipette tip was used to create a linear scratch in the center of the well. Detached cells were gently washed away with PBS, and serum-free medium was added. Images of the scratch were captured at 0 hours and 24 hours to evaluate cell migration and wound closure.

Transwell migration and invasion assays

Transwell chambers (Corning, USA) were used to assess cell migration and invasion. In a 24-well culture plate, 600 µl of RPMI-1640 medium supplemented with 10% FBS was added to the lower chamber, and the Transwell inserts were placed above. Transfected cells were seeded into the upper chambers in serum-free RPMI-1640 medium. After 24 hours of incubation, migration and invasion were performed as described before [18].

Western blotting analysis

Total proteins were extracted from cells and tissues using RIPA buffer (Beyotime, Shanghai, China) containing PMSF protease inhibitors and quantified using the BCA Protein Assay Kit (Beyotime, Shanghai, China). Proteins were separated by 10% SDS-PAGE and transferred onto nitrocellulose membranes. The membranes were blocked with 5% skim milk for 2 hours at room temperature, followed by overnight incubation at 4°C with the appropriate primary antibodies. Subsequently, the membranes were incubated with horseradish peroxidase (HRP)-conjugated secondary antibodies for 2 hours at room temperature. Anti-FBXO22, anti-GAPDH, anti-β-catenin and goat-anti-rabbit secondary antibodies were purchased from Cell Signaling Technology (Danvers, MA, USA). Anti-BAX and anti-BCL-2 antibodies were purchased from Servicebio (Wuhan, China). Anti-CyclinD1 antibody was obtained from Abcam (Cambridge, MA, USA). Anti-c-Myc antibody was purchased from Affinity Biosciences (Jiangsu, China). Protein signals were detected using a Tanon 5200 imaging system (Shanghai, China), and band intensities were quantified with ImageJ software [19].

In vivo experiments

Four- to five-week-old female nude mice were purchased from Changzhou Cavins Laboratory Animal Co., Ltd. (Changzhou, China) and housed under specific pathogen-free (SPF) conditions. To examine the effect of FBXO22 silencing on tumor growth in vivo, KYSE150 cells stably transfected with si-FBXO22 or negative control (NC-FBXO22) were injected subcutaneously into the mice. Tumor growth was monitored weekly for six weeks by measuring tumor volume. At the end of the experiment, all mice were sacrificed, and the tumors were excised, weighed, and used for subsequent protein extraction and analysis.

Statistical analysis

All results are expressed as the means ± standard deviation (SD). Data were analyzed using independent samples t-tests, one-way ANOVA, or chi-square tests where appropriate. A p-value of < 0.05 was considered statistically significant. All experiments were performed in triplicate to ensure reproducibility.

Results

FBXO22 expression and its association with clinical Parameters in ESCA patients

FBXO22 expression in ESCA was analyzed using data from the TCGA database. The results revealed significantly higher FBXO22 expression in ESCA tissues compared to adjacent normal tissues (**Figure 1A**). Further analysis based on clinical parameters demonstrated that FBXO22 was upregulated in tumor samples from both male and female patients relative to their respective normal controls (**Figure 1B**). When stratified by tumor histological subtype, FBXO22 expression was significantly elevated in both esophageal adenocarcinoma and squamous cell carcinoma compared to normal tissues (**Figure 1C**). Additionally, FBXO22 expression was markedly increased across tumor grades 1, 2, and 3 (**Figure 1D**), as well as stag-

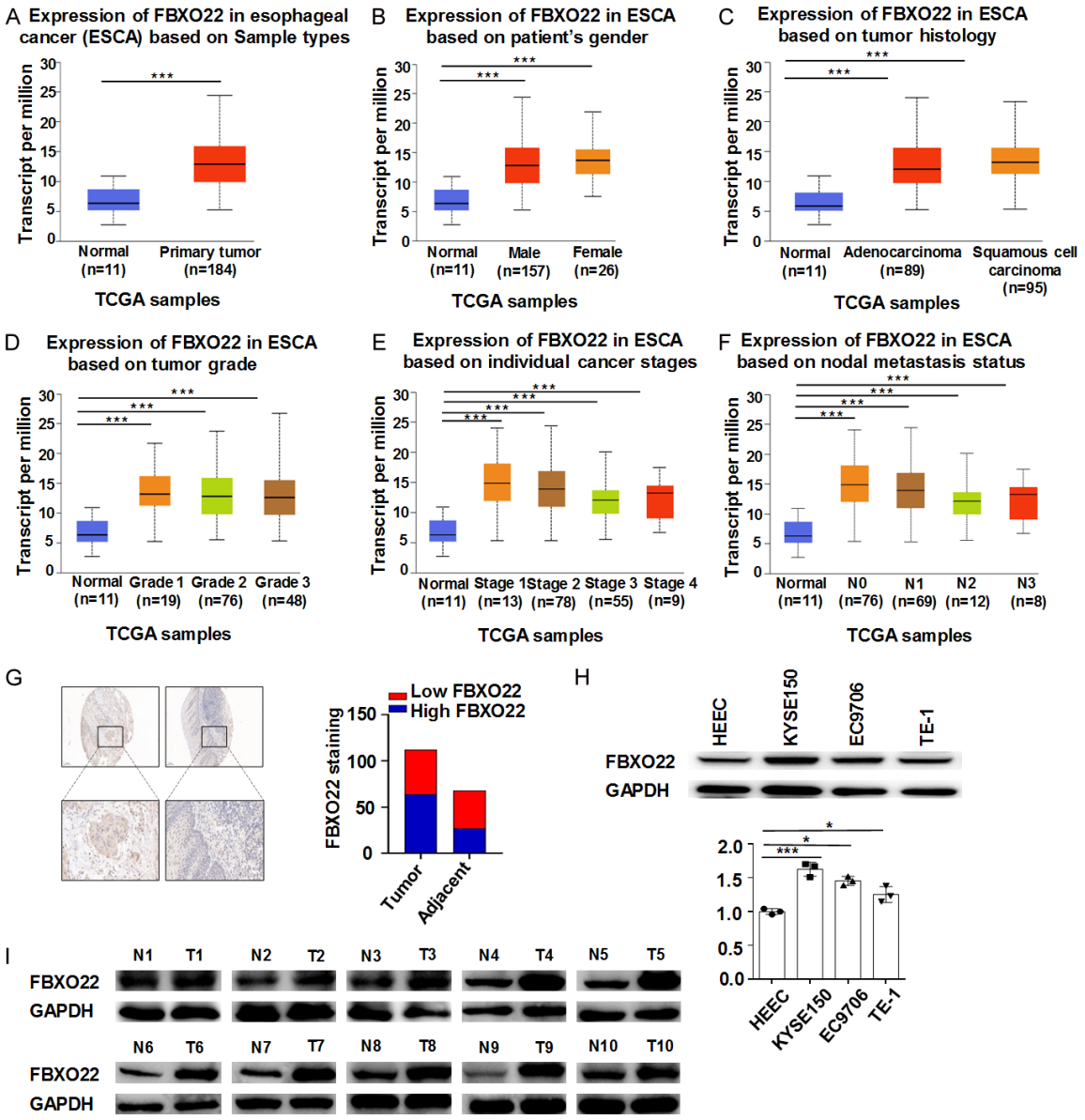


Figure 1. FBXO22 expression is upregulated in ESCA tissues and cells. (A) Analysis of FBXO22 expression in ESCA using the TCGA database. (B-F) Box plots illustrating FBXO22 expression across different patient subgroups based on clinical parameters, including gender (B), tumor histology (C), tumor grade (D), cancer stage (E), and metastasis status (F). N0: no regional lymph node metastasis; N1: 1 - 3 axillary lymph node metastasis; N2: 4 - 9 axillary lymph node metastasis; N3: 10 or more axillary lymph node metastasis. *P < 0.05, **P < 0.01, ***P < 0.001. (G) Immunohistochemical analysis of FBXO22 protein expression in ESCA tissues and matched adjacent paracancerous tissues. (H, I) Western blot analysis of FBXO22 protein expression in ESCA cell lines and tissue samples. * *P* < 0.05, *** *P* < 0.001 compared to the negative control. N: paracancerous tissue; T: tumor tissue.

es 1 through 4 (**Figure 1E**), indicating a progressive rise in expression with advancing disease severity. Moreover, analysis of nodal metastasis status revealed that FBXO22 expression was significantly higher in patients categorized as N0, N1, N2, and N3, suggesting a potential association with lymph node involvement (**Figure 1F**).

FBXO22 expression is upregulated in ESCA tissues and cell lines

Tumor immunostaining analysis was conducted on 68 esophageal paracancer tissues and 112 esophageal cancer tissues. The results revealed that FBXO22 was predominantly localized in the cytoplasm. High FBXO22 expression

was observed in 15 (22.05%) paracancer tissues and 68 (60.71%) ESCA tissues (**Figure 1G**). To further evaluate FBXO22 expression, Western blot analysis was performed on clinical tissue samples, normal esophageal epithelial cells, and esophageal cancer cell lines (**Figure 1H**, **1I**). The results showed that FBXO22 expression was higher in ESCA tissues compared to parancancrous tissues (**Figure 1I**). Moreover, in ESCA cell lines KYSE150, EC9706, and TE-1, FBXO22 expression was markedly elevated compared to normal esophageal epithelial cells (HEEC) (**Figure 1H**).

Silencing FBXO22 inhibits proliferation of ESCA cells

To examine the potential role of FBXO22 in ESCA cells, we performed knockdown and overexpression experiments in KYSE150 and EC9706 cell lines. RT-PCR results showed that siRNA transfection reduced FBXO22 mRNA levels, while FBXO22 plasmids increased its mRNA levels in both cell lines (**Figure 2A**). Western blot analysis confirmed the effective downregulation and upregulation of FBXO22 protein levels (**Figure 2B**, **2C**). To assess the impact of FBXO22 on cell proliferation, we conducted CCK8 assays. The results demonstrated that silencing FBXO22 inhibited cell viability, while FBXO22 overexpression enhanced ESCA cell viability (**Figure 2D**).

Downregulation of FBXO22 promotes apoptosis

The impact of FBXO22 expression on apoptosis in ESCA cells was assessed using flow cytometry and Western blot analysis. Silencing FBXO22 increased the apoptosis rate in ESCA cells compared to the control group (**Figure 3A**). Conversely, FBXO22 overexpression inhibited apoptosis of ESCA cells (**Figure 3B**). FBXO22 overexpression decreased the pro-apoptotic protein BAX expression and increased the anti-apoptotic protein BCL-2 levels in ESCA cells (**Figure 3C**). When FBXO22 was silenced, BAX expression was increased, and BCL-2 expression was decreased (**Figure 3D**). These results suggest that FBXO22 regulates apoptosis in ESCA cells.

Downregulation of FBXO22 inhibits migration and invasion of ESCA cells

To determine whether FBXO22 affected the migratory and invasive abilities of ESCA cells, wound healing assays were performed in EC9706 and KYSE150 cells following FBXO22 knockdown or overexpression. Silencing FBXO22 delayed wound closure, indicating reduced migration in both cell lines (**Figure 4A**). In contrast, upregulation of FBXO22 enhanced wound closure, promoting migration (**Figure 4B**). To further confirm these findings, Transwell migration and invasion assays were conducted. Silencing FBXO22 inhibited both migration and invasion in ESCA cells, while FBXO22 overexpression enhanced these abilities (**Figure 4C**, **4D**). These results collectively indicate that FBXO22 plays a crucial role in controlling the migration and invasion of ESCA cells.

Silencing FBXO22 inhibits the Wnt/β-catenin signaling pathway

We examined the impact of FBXO22 on the Wnt/β-catenin signaling pathway by analyzing the levels of β-catenin and proliferation-related proteins c-Myc and Cyclin D1 through Western blot analysis. The results showed that silencing FBXO22 led to a significant reduction in β-catenin levels, accompanied by decreased expression of c-Myc and Cyclin D1 (**Figure 5A**). Conversely, overexpression of FBXO22 increased β-catenin levels and enhanced the expression of c-Myc and Cyclin D1 (**Figure 5B**). These findings indicate that FBXO22 modulates the Wnt/β-catenin signaling pathway, thereby influencing cell proliferation.

β-catenin knockdown reverses the oncogenic effects of FBXO22 overexpression on cell viability, migration, and invasion

To investigate whether FBXO22 regulates ESCA cell behavior through the β-catenin signaling pathway, we silenced β-catenin in ESCA cells following FBXO22 overexpression. Western blotting analysis further confirmed that β-catenin knockdown abolished the upregulation of β-catenin protein levels induced by FBXO22 overexpression in KYSE150 cells (**Figure 5C**). Knockdown of β-catenin reduced the viability of KYSE150 cells. Moreover, β-catenin silencing reversed FBXO22 overexpression-mediated increase in cell viability (**Figure 5D**). Next, we assessed the effects on cell motility using Transwell assays. β-Catenin knockdown suppressed both migration and invasion of KYSE150 cells and effectively counteracted the pro-migratory and pro-invasive effects driven by FBXO22 overexpression (**Figure 5E**).

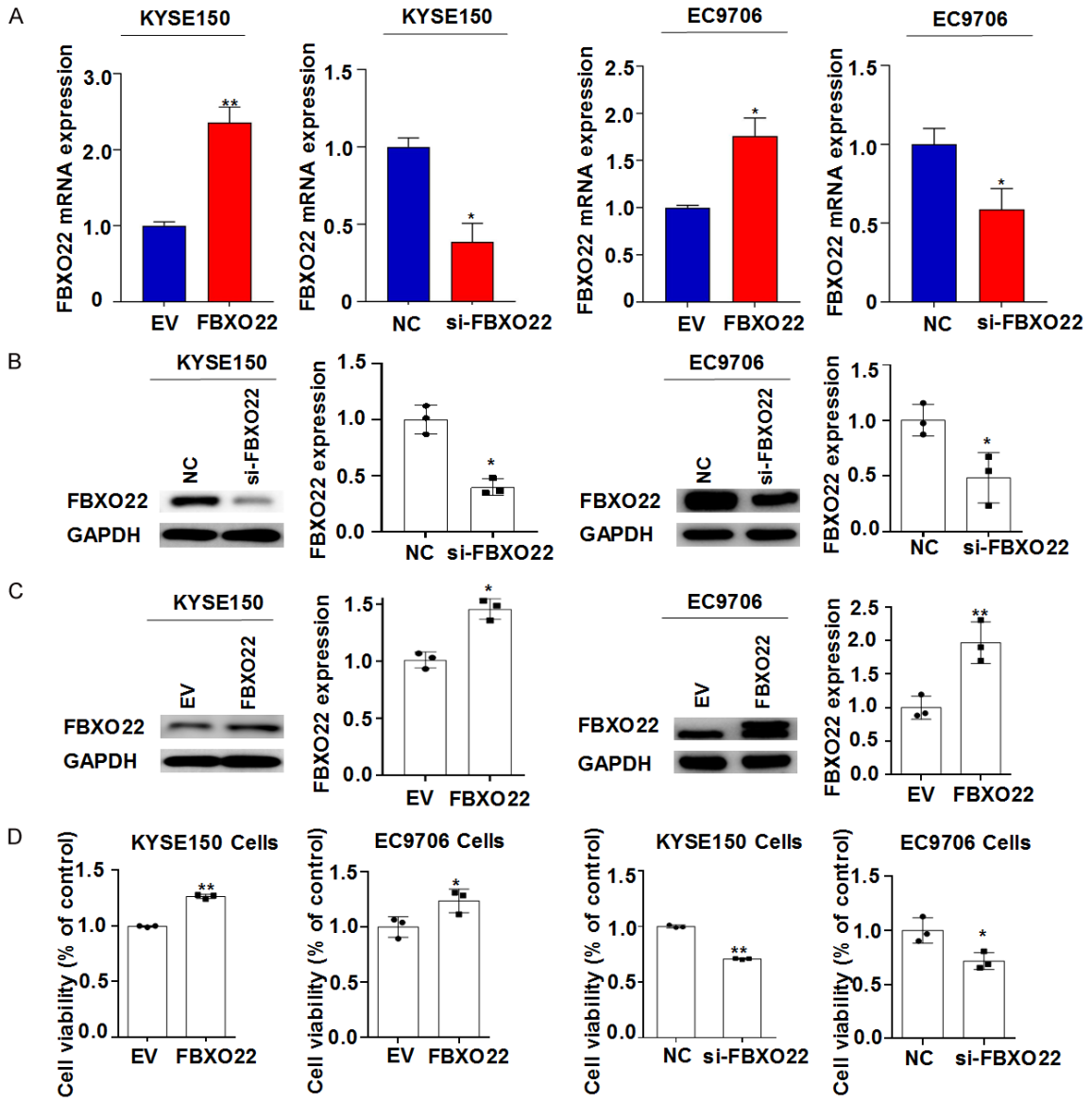
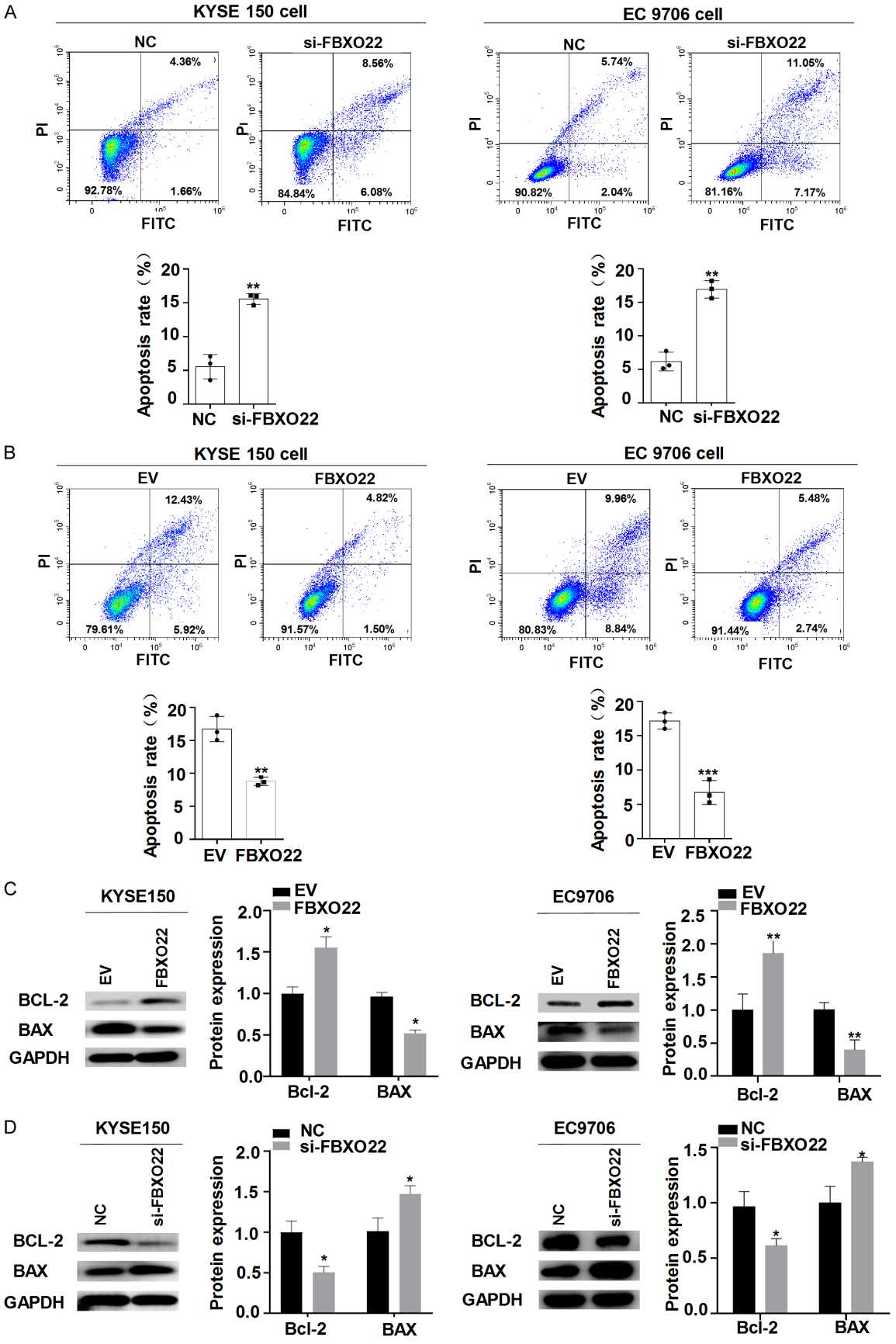


Figure 2. Silencing FBXO22 inhibits the proliferation of ESCA cells. A: qRT-PCR was used to detect the mRNA expression levels of FBXO22 in KYSE150 and EC9706 cells following transfection with FBXO22 siRNA or FBXO22 overexpression plasmid. B: Western blot analysis of FBXO22 protein levels in KYSE150 and EC9706 cells following transfection with FBXO22 siRNA. C: Western blot analysis of FBXO22 protein levels in KYSE150 and EC9706 cells following transfection with FBXO22 overexpression plasmid. D: CCK8 assay was performed to evaluate the effect of FBXO22 upregulation or downregulation on the proliferation of KYSE150 and EC9706 cell lines. *P < 0.05, ** *P* < 0.01 compared with EV (empty vector) or NC (negative control).

Collectively, these results indicate that FBXO22 enhances proliferation, migration, and invasion of esophageal cancer cells, at least in part, through activation of the β-catenin signaling pathway.

Silencing FBXO22 inhibits tumor growth of ESCA in vivo

To investigate the effect of FBXO22 on tumor growth in vivo, we performed a xenograft experiment using nude mice implanted with ESCA cells. Tumor growth in the FBXO22-silenced group was significantly slower compared to the control group (**Figure 6A**). Additionally, tumor weight and volume in the FBXO22-silenced group were notably lower than those in the control group (**Figure 6A**). Western blot analysis of tumor tissues revealed reduced FBXO22 protein expression in the silenced group compared to the control group (**Figure 6B**). These findings demonstrate that


A
KYSE 150 cell
NC
si-FBXO22
4.36%
92.78%
1.66%
8.56%
84.84%
6.08%
PI
FITC
EC 9706 cell
5.74%
90.82%
2.04%
11.05%
81.16%
7.17%
Apoptosis rate (%)
NC
si-FBXO22
B
KYSE 150 cell
EV
FBXO22
12.43%
79.61%
5.92%
4.82%
91.57%
1.50%
EC 9706 cell
9.96%
80.83%
8.84%
5.48%
91.44%
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C
KYSE150
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Figure 3. Downregulation of FBXO22 promotes apoptosis in ESCA cells. A, B: Flow cytometry was used to detect the effect of FBXO22 downregulation or upregulation on apoptosis in ESCA cell lines KYSE150 and EC9706. C, D: Western blot analysis was used to detect the expression levels of apoptotic proteins in ESCA cells following FBXO22 downregulation or overexpression. *P < 0.05, **P < 0.01, ***P < 0.001 compared with EV (empty vector) or NC (negative control).

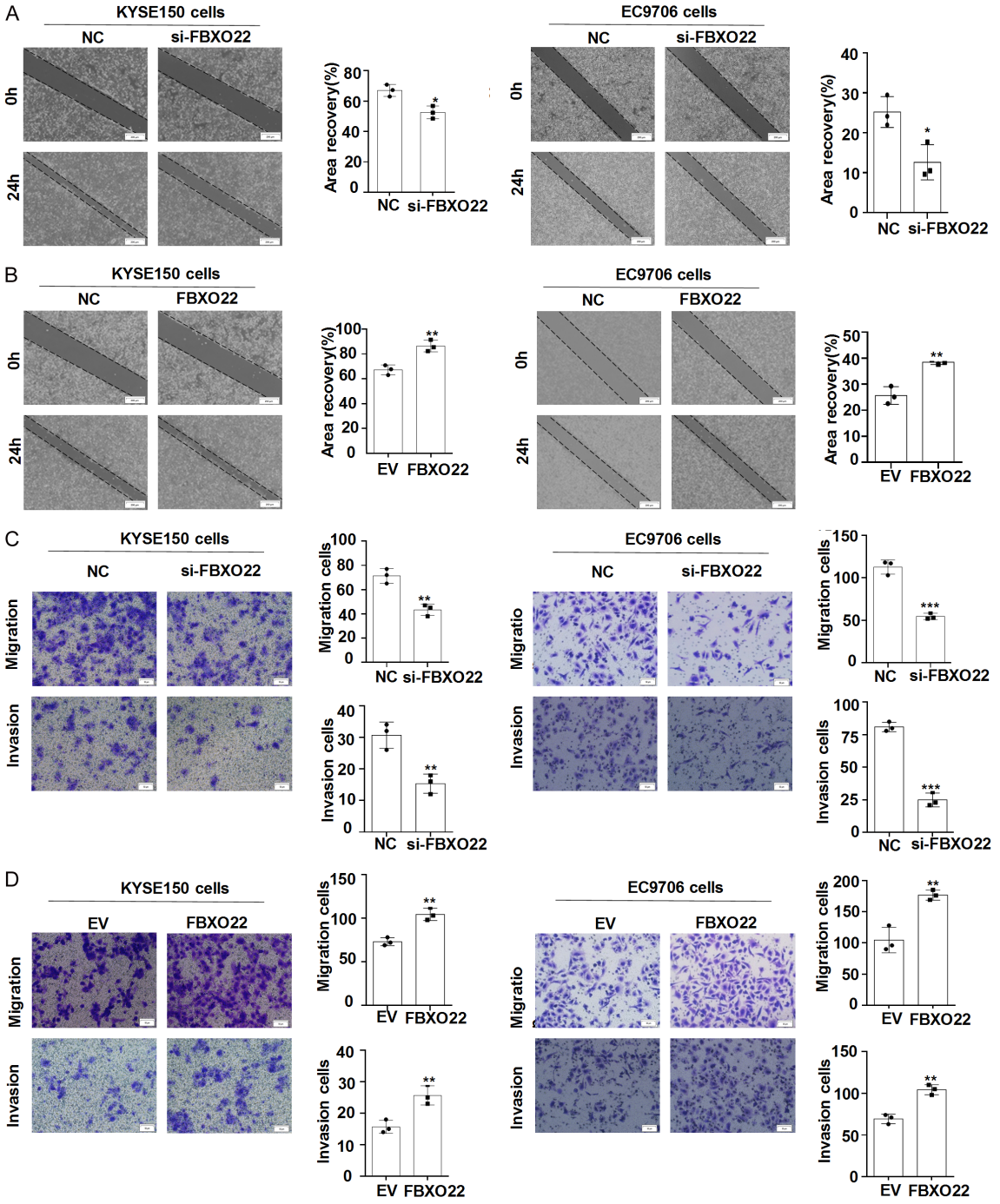

Figure 4. Downregulation of FBXO22 inhibits migration and invasion of ESCA cells. A, B: Wound healing assay demonstrating the effect of FBXO22 downregulation or overexpression on the wound closure ability of KYSE150 and EC9706 cell lines. C, D: Transwell assays showing the impact of FBXO22 downregulation or overexpression on migration and invasion abilities in KYSE150 and EC9706 cell lines. *P < 0.05, **P < 0.01 compared with EV or NC.

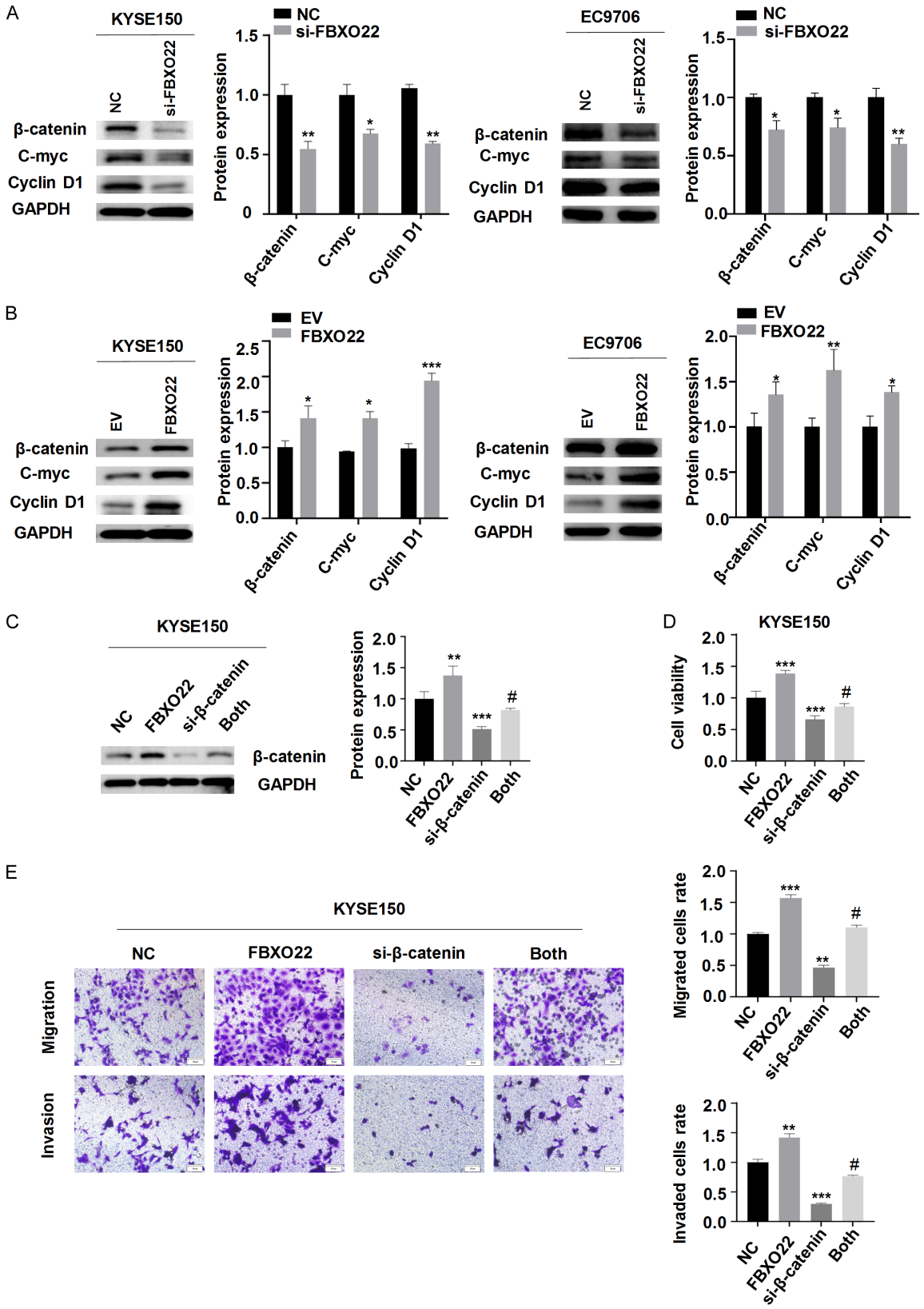

Figure 5. Silencing FBXO22 inhibits the Wnt/β-catenin pathway A: Western blot analysis of the effects of FBXO22 silencing on the Wnt/β-catenin signaling pathway and downstream proteins (β-catenin, Cyclin D1, and c-Myc) in KYSE150 and EC9706 cell lines. B: Western blot analysis of the effects of FBXO22 overexpression on the Wnt/β-

catenin signaling pathway and downstream proteins in KYSE150 and EC9706 cell lines. *P < 0.05, **P < 0.01 compared with EV or NC. C: Western blot analysis of β-catenin expression in KYSE150 cells after co-transfection with FBXO22 cDNA and β-catenin siRNA. D: Cell viability in KYSE150 cells was assessed using the CCK-8 assay following co-transfection with FBXO22 cDNA and β-catenin siRNA. ***P < 0.001 versus NC; #P < 0.05 versus either β-catenin siRNA alone or FBXO22 cDNA alone. NC: non-specific control siRNA; FBXO22: FBXO22 cDNA; si-β-catenin: β-catenin siRNA; Both: co-transfection of FBXO22 cDNA and β-catenin siRNA. E: Cell migration and invasion were evaluated by Transwell assays in KYSE150 cells following co-transfection with FBXO22 cDNA and β-catenin siRNA. ***P < 0.001 versus NC; **P < 0.01 versus NC; #P < 0.05 versus either β-catenin siRNA alone or FBXO22 cDNA alone.

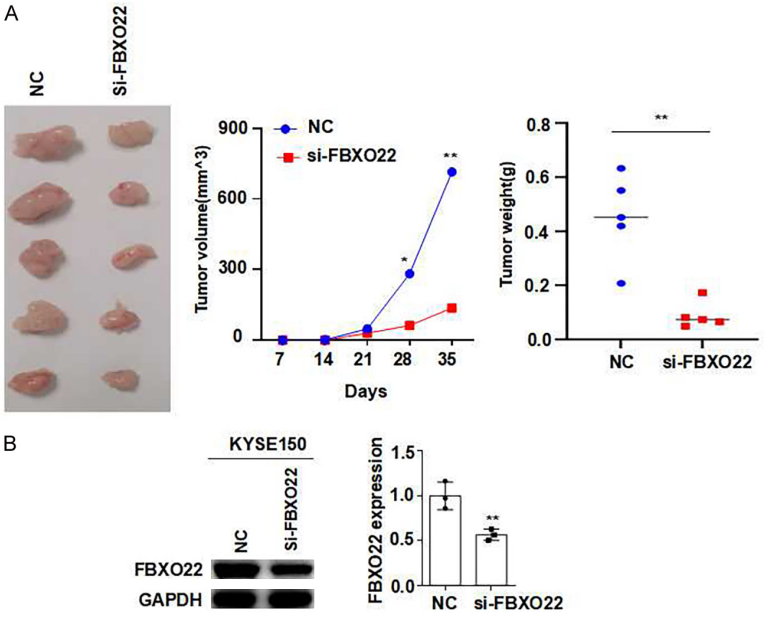

Figure 6. Silencing FBXO22 inhibits tumor growth in ESCA in vivo. A: Graphical representation of tumorigenic outcomes in nude mice injected with KYSE150 cells transfected with NC (negative control) or Si-FBXO22. B: Western blot analysis and semi-quantitative assessment of FBXO22 protein expression in tumor tissues from the NC and Si-FBXO22 groups. **P < 0.01 compared with the negative control.

silencing FBXO22 can effectively suppress tumor growth in vivo.

Discussion

Accumulating evidence indicates that FBXO22 plays an essential role in the progression of human cancer [24]. For example, FBXO22 exhibits a dual role in the development and progression of breast cancer. On one hand, HDM2 overexpression promotes p53 degradation, leading to FBXO22 deficiency, which enhances the migration and invasiveness of breast cancer cells. On the other hand, FBXO22 is highly expressed in primary breast cancers, where it promotes cell proliferation, colony formation in vitro, and xenograft tumor formation in vivo [25, 26]. In ovarian cancer, FBXO22 expression is elevated in tumor tissues compared to paraneoplastic tissues. High FBXO22 expression has been found to promote ovarian cancer cell proliferation in vitro, suggesting a role in ovarian carcinogenesis. Furthermore, FBXO22 expression levels in ovarian cancer tissues correlate with the stage and grade of the disease [27]. In renal cancer, however, FBXO22 expression is significantly lower in tumor tissues compared to normal kidney tissues. Interestingly, while FBXO22 expression does not influence renal cancer cell proliferation, it appears to inhibit infiltration and metastasis of renal tumor cells [28]. These studies highlight the diverse roles of FBXO22 in various cancers, functioning as either a promoter or inhibitor of tumor progression depending on the cancer type. Despite this growing body of research, the role of FBXO22 in ESCA remains poorly understood. Therefore, this study focuses on elucidating the effect of FBXO22 on ESCA development and progression.

First, we demonstrated that FBXO22 expression was upregulated in ESCA tissues and cell lines compared to normal tissues and cells. Silencing FBXO22 markedly inhibited the growth of ESCA cell lines KYSE150 and EC9706, whereas overexpression of FBXO22 promoted their growth. These findings align with previous studies in lung cancer [29]. Furthermore, we observed that alterations in FBXO22 expression affected the levels of BAX and BCL-2, two proteins that regulate programmed cell death and apoptosis. The disruption of the balance between pro-apoptotic (BAX) and anti-apoptotic (BCL-2) proteins can significantly influence

cell survival and apoptosis [30]. Tumor metastasis is a common and lethal feature of ESCA, contributing to 90% of cancer-related deaths. Metastasis involves the invasion of surrounding tissues and spread of tumor cells to distant sites through blood or lymphatic system. This process relies on critical steps, including cell migration and invasion [31, 32]. In our study, FBXO22 overexpression significantly increased the migration and invasion of ESCA cells, while silencing FBXO22 reduced this ability. These findings suggest that FBXO22 promotes tumor growth and metastasis in ESCA.

The Wnt signaling pathway, particularly the Wnt/β-catenin pathway, is a highly conserved signaling cascade involved in cellular communication [33, 34]. Activation of the Wnt/β-catenin pathway reduces the phosphorylation of β-catenin, leading to its accumulation in the cytoplasm and subsequent translocation to the nucleus. In the nucleus, β-catenin activates the transcription of downstream target genes, such as Cyclin D1 and c-Myc, which are critical for cell proliferation and tumorigenesis [35]. Aberrant expression of Cyclin D1 and c-Myc is associated with various aspects of tumorigenesis, including uncontrolled cell cycle progression, enhanced proliferation, migration, and malignant transformation [36]. One study has shown that deregulation of the Wnt/β-catenin signaling pathway is often accompanied by the development and progression of malignancies, including esophageal cancer [37]. Our study revealed that upregulation of FBXO22 promoted β-catenin expression, accompanied by increased levels of Cyclin D1 and c-Myc. This activation of the Wnt/β-catenin pathway may partly explain the pro-tumorigenic effects of FBXO22. These findings suggest that FBXO22 may play a pivotal role in esophageal cancer by regulating key pathways that promote tumor growth, migration, and invasion.

Conclusion

In summary, our study demonstrated that FBXO22 expression is upregulated in ESCA tissues. Downregulation of FBXO22 inhibited cell viability, migration and invasion while promoting apoptosis in ESCA cells, whereas upregulation of FBXO22 exhibited the opposite effects. Additionally, silencing FBXO22 suppressed tumor growth in a nude mouse model. Mechanistically, FBXO22 was found to regulate the WNT/β-catenin signaling pathway, highlighting its role in promoting tumorigenesis. These findings suggest that FBXO22 could serve as a potential therapeutic target for ESCA.

Acknowledgements

The research was supported by the major project from The Key Project of Natural Science Foundation of Anhui Provincial Department of Education (No. 2022AH051528, KJ2021ZD-0080) and the Innovation Training Project for College Students in Anhui province (S20211-0367132).

Disclosure of conflict of interest

None.

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