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Downregulation of long non-coding RNA DUXAP10 inhibits proliferation, migration, and invasion of renal cell carcinoma

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Abstract. – OBJECTIVE: Renal cell carcinoma (RCC) is the most common kidney malignancy that frequently leads to metastasis. Increasing evidence has shown that long non-coding RNAs (lncRNAs) play crucial roles affecting the progression of RCC. The role of lncRNA DUXAP10 in the evolution of RCC has not been defined yet. This project was designed to clarify the effects of DUXAP10 on the proliferation and tumorigenesis of RCC.

PATIENTS AND METHODS: We examined the expression of DUXAP10 in the Cancer Genome Atlas (TCGA) and ONCOMINE oncology databases. Then, we performed quantitative reverse-transcription polymerase chain reaction (qRT-PCR) to evaluate DUXAP10 expression in human RCC tissues and cell lines. The correlation between the expression of DUXAP10 and clinical characteristics of RCC patients was analyzed by univariate and Kaplan–Meier analyses. To unveil the biological function of DUXAP10 in cell cycle progression, cell growth, and invasion of RCC, we conducted knockdown experiments *in vitro*. qRT- PCR and western blotting assays were performed to further investigate the function of DUXAP10 in cancer biology.

RESULTS: The data from TCGA showed that the expression of DUXAP10 was upregulated in tissues of RCC compared with normal tissues. Moreover, ONCOMINE database analysis indicated that high DUXAP10 levels were correlated with high clinical stages, inferior TNM classification, and poor overall survival. Furthermore, the results indicated that knockdown of DUXAP10 remarkably inhibited the RCC cell growth, mobility, and invasion, in association with the downregulation of cyclin D, cyclin E, CDK4, N-cadherin, E-cadherin, and vimentin.

CONCLUSIONS: Our findings highlight the oncogenic role of DUXAP10 in RCC and that DUXAP10 may serve as a novel predictive biomarker and therapeutic target for RCC.

Key Words:
Renal cell carcinoma, Long noncoding RNAs, Metastasis, EMT, Biomarker.

Abbreviations

OD: optical density; NC: negative control; qRT-PCR: quantitative reverse-transcription polymerase chain reaction.

Introduction

Recent studies show that the incidence of renal cell carcinoma (RCC) is increasing worldwide, with about 400,000 new patients diagnosed in 2018[1]. In addition, RCC accounts for a great percentage of adult malignancies. Indeed, RCC frequently leads to metastasis, being the most lethal urological cancer[2-4]. During the past two decades, methods for staging, diagnosis, and treatment of RCC patients have significantly advanced. However, conventional therapies, such as radiotherapy and chemotherapy, have a low curative effect in patients with metastatic RCC[5]. Moreover, reliable biological markers for the initial diagnosis of RCC and patient prognostic estimation are still lacking[6]. Therefore, understanding the mechanisms that control the progression and metastasis of RCC is a key step in developing better therapeutic and diagnostic methods.

Long non-coding RNAs (lncRNAs) are a new class of transcripts with limited coding potential and length that exceeds 200 nucleotides[7]. They play a critical role in cancer development and progression[8] by interacting with cognate protein or RNA partners, thus modifying the transcriptional or post-transcriptional processing of key signaling proteins[9,10]. Recently, several lncRNAs have been shown to regulate the progression of RCC. In particular, *EGFR-AS1* promoted

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RCC proliferation and invasion by affecting the stability of *EGFR* mRNA[11]. *MALAT1* was reported to be upregulated in RCC tissues and control the proliferation and apoptosis of RCC by interacting with miR-205 *in vivo*[12]. *LINC-PINT* was identified to be frequently upregulated in RCC samples and cell lines and to promote their proliferation through EZH2[13]. Therefore, lncRNAs may be a valuable resource for better understanding the mechanisms that underlie the occurrence and progression of RCC.

DUXAP10 is a novel lncRNA that belongs to the DUXA homeobox gene family[14]. The genomic location of *DUXAP10* gene is 14p11.2. Increasing evidence supports that *DUXAP10* plays an important role in the initiation and progression of various types of cancers. Previously, our group has investigated the function of *DUXAP10* in prostate cancer[15]. However, the role of *DUXAP10* in RCC remained unidentified. We thus hypothesized that high *DUXAP10* levels would correlate with poor patient prognosis and distant RCC metastasis. We identified that the expression of *DUXAP10* was markedly increased in RCC. Moreover, statistic data supported that *DUXAP10* was positively correlated with certain clinical parameters, including gender, clinical stage, and distant metastasis. Then, we found that downregulating *DUXAP10* could decrease the expression of N-cadherin and increase E-cadherin levels. Altogether, these observations revealed that *DUXAP10* promoted RCC tumorigenesis through epithelial-mesenchymal transition (EMT).

Patients and Methods

Human Tissue Samples and Cell Lines

In our study, we followed the European Association of Urology Guideline on renal cell carcinoma for the inclusion or exclusion of patients (uroweb.org/guideline/renal-cell-carcinoma). A total of 18 paired RCC specimens were collected from the Urology Department of Peking University Shougang Hospital between February and July 2018. Informed consent was granted by all patients. Collected tissues were instantly conserved in liquid nitrogen. All experiments were approved by the Ethics Committee of Peking University Shougang Hospital. The RCC cell lines 786-O and A498, and normal kidney epithelial cells (HKC) were purchased from China Infrastructure of Cell Line Resource (Haidian, Beijing, China). HKC and A498 cells were cultured in Dulbecco's Modified Eagle's Medium (Gibco, Thermo Fisher Scientific, Waltham, MA, USA). 786-O cells were cultured in Roswell Park Memorial Institute-1640 (Gibco, Thermo Fisher Scientific, Waltham, MA, USA). All media were supplemented with 10% fetal bovine serum (Gibco, Thermo Fisher Scientific, Waltham, MA, USA).

RNA Isolation and Quantitative PCR

Total RNA was extracted from tissues and cells using TRIzol reagent (Invitrogen, Carlsbad, CA, USA). Next, cDNA synthesis and qPCR were performed according to Minimal Information for Publication of Quantitative Real-Time PCR Experiments (MIQE) guidelines, as previously described[16]. *GAPDH* was chosen as an internal control. mRNA expression levels were relatively assessed using the 2-ΔΔCt method. The specific primers for PCR were as follows: *GAPDH* forward, 5′-AGATCATCAGCAATGCCTCCT-3′; *GAPDH* reverse, 5′-TGAGTCCTTCCACGATACCAA-3′; *DUXAP10* forward, 5′-GGTTCAACAGTATGGCTCCAAAG-3′; *DUXAP10* reverse, 5′-GACTGCCCATCCACAGATGAAG-3′; *E-cadherin* forward, 5′-TGCTAATTCTGATTCTG CTGCTCT-3′; *E-cadherin* reverse, 5′-CAAGTCAAAGTCCTG GTCCTCT-3′; *N-cadherin* forward, 5′-ATCCTGCTTATCCTTGT GCTGA-3′; *N-cadherin* reverse, 5′-CATAGTCCTGGTCTTC TTCTCCTC-3′; and *vimentin* forward, 5′-GCCCTAGACGAACTGGGTC-3′; *vimentin* reverse, 5′-GGCTGCAACTGCCTAATGAG-3′.

Cell Transfection

The sequences of small interfering RNA (siRNA) for transient transfection assays were as follows:

si-DUXAP10-1: 5′-CAGCAUACUUCAAAUUCACAGCAAA-3′; *si-DUXAP10-2*: 5′-AGUUGUUUGUUAGAAUACUGGUGCU-3′; and *si-DUXAP10-3*: 5′-GGAACUUCCCAAACCUCCAUGAUUU-3′.

These oligonucleotides were transfected into A498 and 786-O cells using Lipofectamine 2000 (Invitrogen, Carlsbad, CA, USA), based on the manufacturer protocol. Cells were harvested for qPCR and Western blotting 48 h and 72 h post-transfection, respectively.

CCK-8 Assay, Clone Assay, and Cell Cycle Analysis

Cell viability was determined using the CCK-8 assay. RCC cells were seeded in 96-well plates at a density of 2×10^3 cells/well. The cell viability was assessed using the CCK-8 Assay Kit (Dojindo Molecular Technologies, Kumamoto, Japan), according to the manufacturer's instructions. Finally, the absorbance was measured at 450 nm on a micro-

plate reader Multiskan FC (Thermo Fisher Scientific, Waltham, MA, USA). The colony formation assay revealed the clonogenic capacity of cancer cells to evaluate the cell viability. Moreover, the cell cycle also plays a crucial part in cell growth. The details of colony formation and cell cycle assays have been presented in our previous paper.[16]

Apoptosis Analysis

To detect cell apoptosis, A498 and 786-O cells were harvested 48 h post-transfection and washed with PBS. Then, Annexin V-FITC (Invitrogen, Carlsbad, CA, USA) was added to the cell suspension, according to the manufacturer's recommendations. Finally, cells were stained with propidium iodide (eBioscience, Invitrogen, Carlsbad, CA, USA) and submitted for analysis on a flow cytometer (BD Biosciences, San Jose, CA, USA).

Wound Healing, Migration, and Invasion Assays

The wound healing and transwell assays allow the study of cell migration and cell-cell interactions. These analyses were performed according to our previous protocols[16]. Cell invasion assays were conducted to detect the invasion capacity of RCC cells. Cell invasion was measured on 24-well transwell chambers with 8 μm Milicell inserter (Millipore, Merck KGaA, Darmstadt, Germany) with Matrigel (BD Biosciences, San Jose, CA, USA). We seeded 1×10^5 cells in serum-free medium. Whereas The lower chamber contained media with 10% bovine calf serum (BCS). Cells from the upper chamber were fixed with 4% paraformaldehyde after 36 h. The number of cells on the lower side was measured under a microscope. Different fields were randomly selected for average counting.

Western Blotting

Western blotting was conducted to determine the change in protein level. Primary antibodies specific for cyclin D, cyclin E, CDK4, N-cadherin, E-cadherin, vimentin, and β-actin were purchased from Cell Signaling Technology (Cell Signaling Technology, Danvers, MA, USA). The immunoblots were visualized using enhanced chemiluminescence (Santa Cruz Biotechnology, Santa Cruz, CA, USA). All other reagents and chemicals were purchased from Sigma. All optional processes were based on the manufacturer protocols from Cell Signaling Technology (https://www.cst-c.com).

Statistical Analysis

SPSS 20.0 (IBM Corporation, Armonk, NY, USA) was used for all statistical analyses. A two-sided paired Student's *t*-test was used for comparisons between two groups. $p < 0.05$ indicated a statistically significant difference.

Results

DUXAP10 is Upregulated in Renal Cell Carcinoma

In the present study, we firstly analyzed the expression of *DUXAP10* in a cohort of 72 paired RCC samples and adjacent normal tissues from the whole transcriptome database of TCGA. We found high expression of *DUXAP10* in RCC tissues compared with normal tissues ($p < 0.01$, Figure 1A), implying a latent positive link between the expression level of *DUXAP10* and RCC. To further validate this link, we performed qPCR assays to examine the expression of *DUXAP10* in a cohort of 18 paired clinical samples and found results consistent with our TCGA analysis. ($p < 0.001$) (Figure 1B). Next, to clarify the correlation between *DUXAP10* levels and clinical features, we downloaded and analyzed the RCC clinical data from the Bittner renal dataset in the ONCOMINE oncology database (n=256) (www.oncomine.org). The clinical and demographic feature baseline of these patients is illustrated in Table I. Moreover, the data revealed that higher *DUXAP10* expression levels were significantly correlated with male ($p = 0.001$), advanced pathophysiological stage ($p = 0.002$), larger tumor volume ($p = 0.005$), lymph node invasion ($p = 0.004$), and metastasis ($p = 0.01$) in RCC (Table II). In contrast, *DUXAP10* levels had no correlation with age ($p = 0.901$). The Spearman correlation analysis showed that the expression of *DUXAP10* was correlated with gender ($p = 0.001$), advanced stage ($p = 0.001$), T classification ($p = 0.005$), N classification ($p = 0.004$), and metastasis ($p = 0.01$) (Table III). Additionally, to investigate the association between the level of *DUXAP10* and the patient prognosis in RCC, we downloaded the TCGA renal dataset in the ONCOMINE (n=88). The Kaplan–Meier analysis showed that *DUXAP10* overexpression was linked with a poor overall patient survival (Log-rank test, $p = 0.0037$; Gehan-Breslow-Wilcoxon test, $p = 0.0084$, Figure 1C). Collectively, these results indicated that the expression of *DUXAP10* was upregulated in RCC compared with normal tissues, and that overexpression of *DUXAP10* in

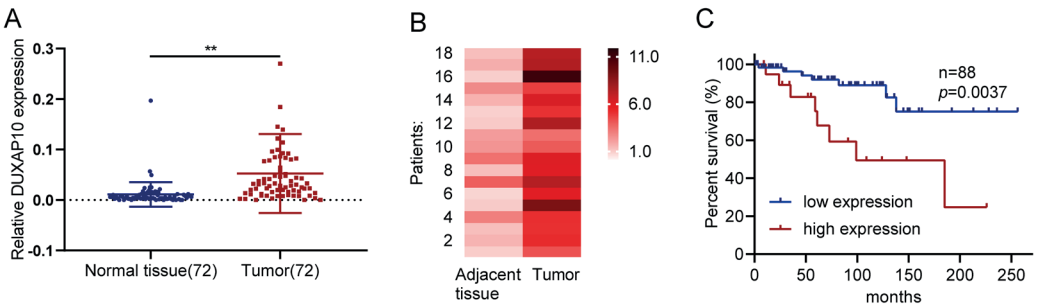

Figure 1. DUXAP10 is upregulated in renal cell carcinoma. **A,** Relative expression of DUXAP10 in RCC patient tissues (n=72) and normal tissues (n=72) in TCGA database. **B,** Relative expression of DUXAP10 in RCC tissues compared with adjacent normal tissues (n= 18) using qRT-PCR and normalized to GAPDH. **C,** Kaplan–Meier and log-rank test for the overall survival curves in 88 RCC patients by high and low expression of DUXAP10 in ONCOMINE oncology database. *$p < 0.05$, ** $p < 0.01$.

primary RCC patients was correlated with poor prognosis.

Knockdown of DUXAP10 Inhibits RCC Cell Proliferation

We first examined the expression level of *DUXPA10* in a panel of human RCC cells and HKC by qRT-PCR analysis. The results revealed that *DUXAP10* levels were notably upregulated in A498 and 786-O cells, compared with the HKC line (Figure 2A). Next, to study the function of *DUXAP10* in RCC, we designed three different *DUXAP10* short interference RNAs (siRNAs) to transfect into these two RCC cell lines. After 48 h, we extracted total RNA, and observed by qRT-PCR that the si-*DUXAP10*-1 and 2 had a higher interfering efficiency than the si-*DUXAP10*-3 (Figure 2B). Thus, we selected si-*DUXAP10*-1 and 2 for subsequent experiments.

A CCK-8 assay was conducted to explore the effect of *DUXAP10* on cellular proliferation. A498 and 786-O cells were transfected with siRNA, and knockdown of *DUXAP10* led to a lower growth rate than that of control cells (Figure 2C, D). To further confirm the effect of *DUXAP10* on cell proliferation, a colony formation assay was conducted, and the result revealed that the silencing of *DUXAP10* significantly decreased the clonogenic capacity of RCC cells (Figure 2E, F). Altogether, these results indicated that *DUXAP10* might possess a vital role for the proliferation and tumorigenicity of RCC cells.

Knockdown of DUXAP10 Promotes Cell-Cycle Arrest and Apoptosis

Cell-cycle dysfunctions may induce tumor cell proliferation. We performed flow cytometry analyses (FCM) to investigate the role of *DUXAP10* in cell cycle progression. As shown in Figure 3A and 3B, transfection of siRNAs in RCC cells led to cell cycle arrest between the G0/1 and S phase. The proportion of cells in the S phase was decreased, indicating that *DUXAP10* may promote the transition for the G1-S phase.

Furthermore, we studied the potential mechanisms underlying cell growth suppression after *DUXAP10* knockdown and evaluated the apoptotic rate by FCM. The results revealed that *DUXAP10* depletion by siRNA-1 and 2 in A498 and

Table I. Clinicopathological characteristics of patient samples and expression of DUXAP10 in renal cell carcinoma.

Characteristics	No. of cases (%)
Age (y)	
< 60	127 (49.6)
≥ 60	129 (50.4)
Gender	
Male	156 (60.9)
Female	100 (39.1)
Clinical stage	
I	183 (71.5)
II	22 (8.6)
III	31 (12.1)
IV	20 (7.8)
T classification	
T1	184 (71.9)
T2	24 (9.4)
T3	47 (18.4)
T4	1 (0.4)
N classification	
N0	248 (96.9)
N1	8 (3.1)
Metastasis	
No	246 (96.1)
Yes	10 (3.9)
Expression of DUXAP10	
Low expression	128 (50.0)
High expression	128 (50.0)

Table II Correlation between *DUXAP10* expression and clinicopathologic characteristics of renal cell carcinoma patients.

	DUXAP10		
Characteristics *DUXAP10*	Low, no. cases	High, no. cases	*p*-value
Age(y)			
< 60	63	64	0.901
≥ 60	65	64	
Gender			
Male	65	91	0.001
Female	63	37	
Clinical stage			
I/II	113	92	0.002
III/IV	15	36	
T classification			
≤ 7 cm	102	82	
> 7 cm	26	46	0.005
N classification			
N0	128	120	0.004
N1	0	8	
Metastasis			
No	127	119	0.01
Yes	1	9	

Table III Spearman correlation analysis between DUXAP10 and clinicopathological characteristics.

	DUXAP10 expression level	
Variables	Spearman correlation	*p*-value
Age	-0.008	0.901
Gender	-0.208	0.001
Clinical stage	0.205	0.001
T classification	0.174	0.005
N classification	0.180	0.004
Metastasis	0.161	0.01

786-O cells significantly increased the early and later apoptotic rates compared to cells belonging to the si-NC groups (Figure 3C, D). Collectively, these results confirmed that *DUXAP10* might drive cell proliferation by promoting cell cycle progression and inhibiting apoptosis.

Since the cell cycle progression has been demonstrated to play a critical role in tumor proliferation, we further investigated the effects of *DUXAP10* silencing on the expression of cell cycle regulators, such as CDK4, cyclin D, and cyclin E. The results uncovered that, 786-O and A498 cells transfected with siRNA-*DUXAP10* significantly decreased the mRNA levels of CDK4, cyclin D, and cyclin E (Figure 3E, F). Western blotting results exhibited a consistent trend in protein expression levels. These results demonstrated that knockdown of *DUXAP10* might lead to cell cycle arrest in G0/G1 by downregulation of CDK4, cyclin D, and cyclin E.

Decreased DUXAP10 Expression Inhibits the Migration and Invasion of RCC

As the migration and metastasis of cancer cells are considered to play crucial roles in cancer progression, migration and invasion-related experiments were conducted. As shown in Figure 4A, the wound healing assays demonstrated that A498 and 786-O cells transfected with siRNA-*DUXAP10* showed lower migration rates compared with the control. Furthermore, transwell assays were conducted to further investigate the role of *DUXAP10* in cellular migration capacity. Similarly, descending trends were observed during wound healing assays (Figure 4B). To clarify the effects of *DUXAP10* on the invasion of RCC cells, we performed a Matrigel-coated invasion assay, and the results indicated that the knockdown of *DUXAP10* impaired the invasion ability of RCC cells (Figure 4C). Since EMT is crucial for carcinoma metastasis, we used qRT-PCR and western blotting to evaluate whether *DUXAP10* could play a role in the metastasis of RCC cells. qRT-PCR results indicated that E-cadherin expression was dramatically upregulated in RCC cells compared with control cells ($p < 0.01$). How-

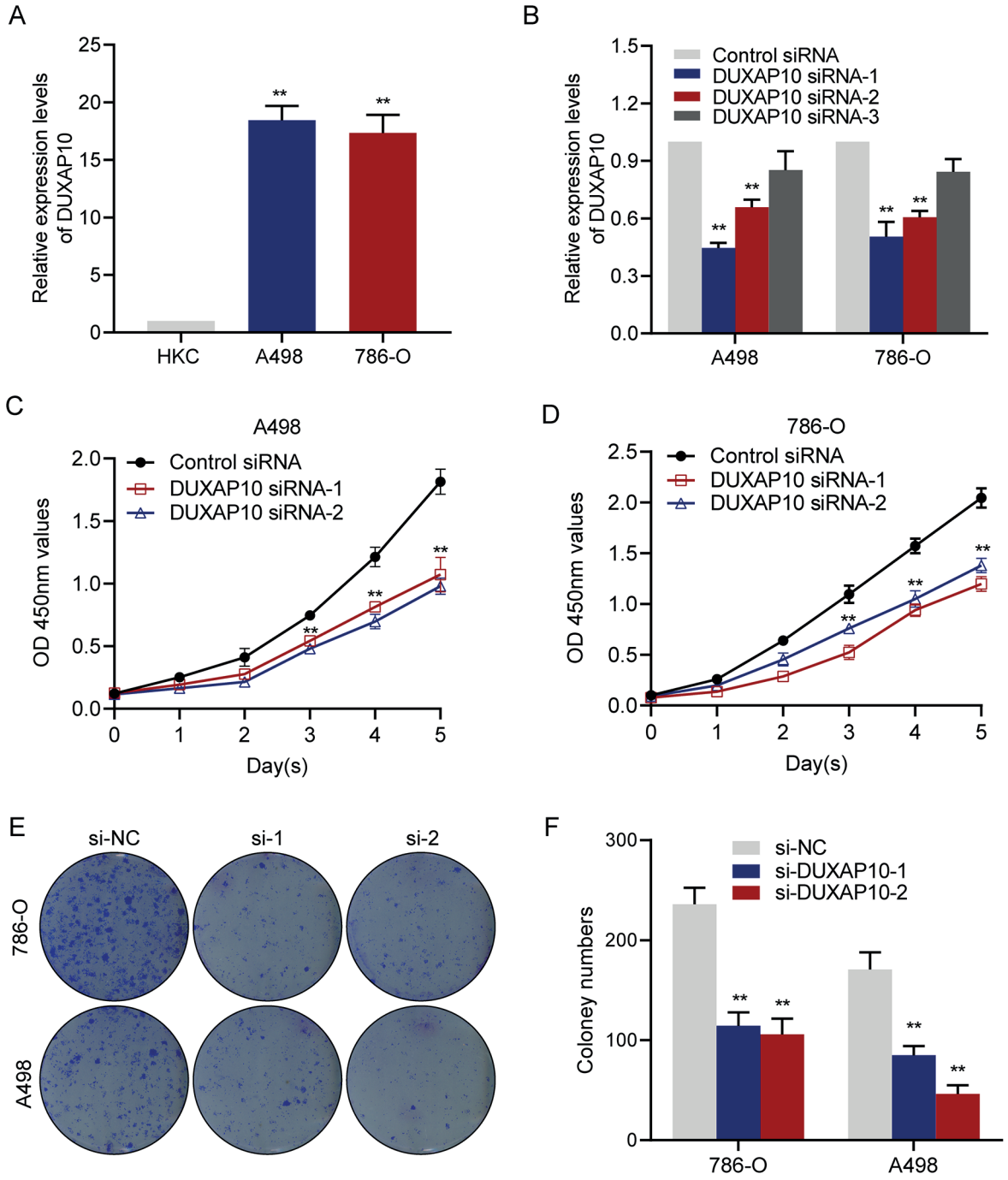

Figure 2. Knockdown of DUXAP10 represses RCC cell proliferation. (A) qRT-PCR was performed to analyze DUXAP10 levels in the RCC and HKC cell lines. GAPDH was used as a reference gene. (B) After transfection with si-NC or si-DUXAP10-1,2,3 for 48 h, the expression of DUXAP10 was measured by qRT-PCR. (C, D) The effects of DUXAP10 knockdown on the proliferation of A498 and 786-O cell lines was evaluated by CCK-8 assay. (E, F) The effects of DUXAP10 knockdown on the proliferation of A498 and 786-O cell lines was evaluated by colony formation assay. qRT-PCR data were expressed as fold change ($2^{-\Delta\Delta CT}$) and evaluated after normalization to the levels of GAPDH in the same samples. *$p < 0.05$, ** $p < 0.01$.

ever, knockdown of *DUXAP10* downregulated N-cadherin and vimentin expression compared to the negative control (Figure 4D). Moreover, western blotting assays revealed that depletion of *DUXAP10* with si-*DUXAP10*-1 and 2 significantly upregulated E-cadherin, while down-

regulating N-cadherin and vimentin in A498 and 786-O cells (Figure 4E). In conclusion, these results suggest that *DUXAP10* might regulate cancer metastasis through EMT.

Discussion

Renal cell carcinoma (RCC) is one of the most common cancers of the urinary system in

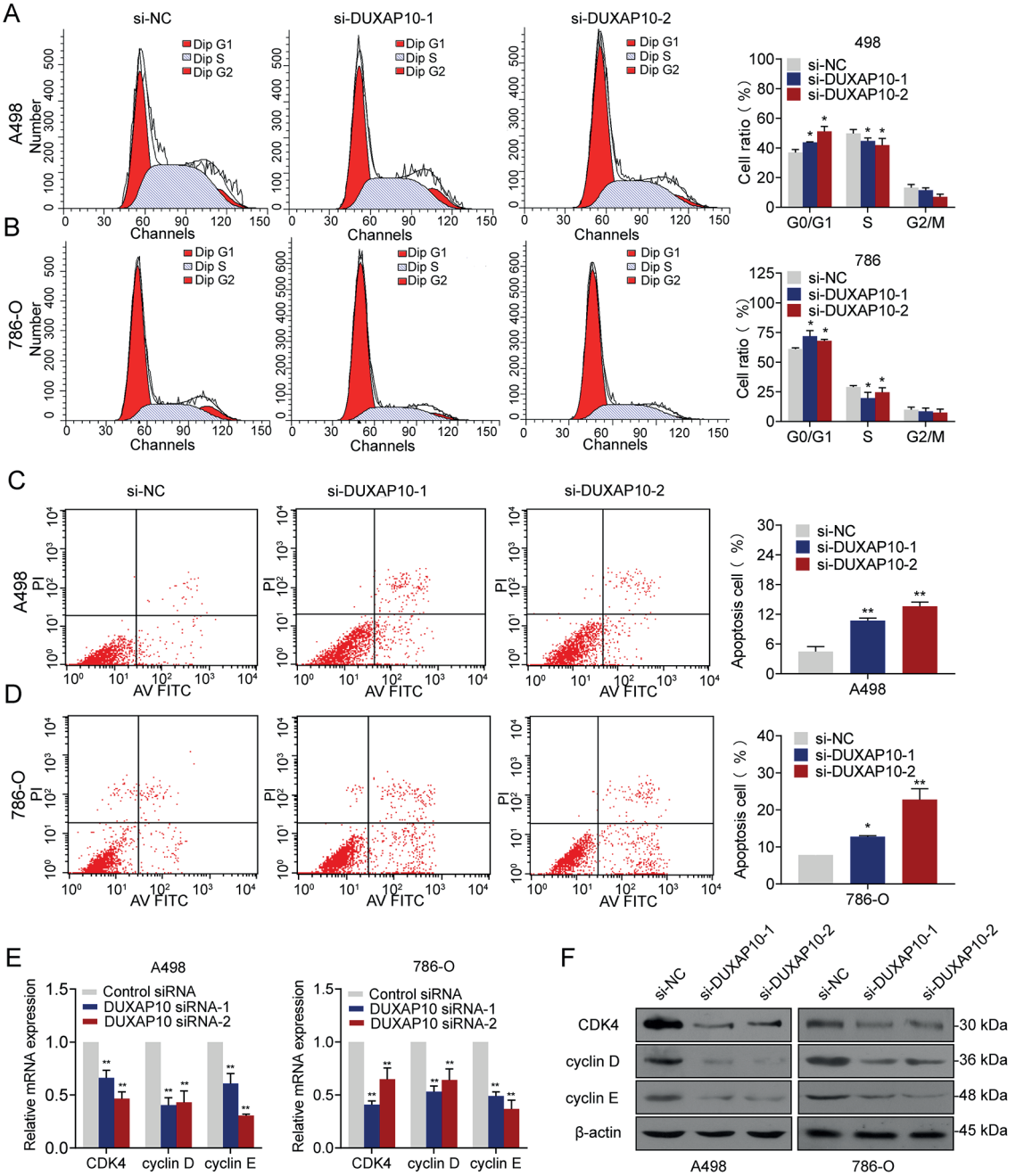

Figure 3. Knockdown of DUXAP10 arrests cell-cycle progress and promotes apoptosis. **A-B,** Left pane: Flow cytometry assays were performed to analyze the cell cycle progression; Right panel: The bar chart indicates the percentage of A498 and 786-O cells in cell-cycle distribution. **C-D,** Left pane: Flow cytometry was performed to detect the rate of apoptotic RCC cells. Right panel: The bar chart indicates the percentage of apoptotic A498 and 786-O cells. **E,** The expression of cell-cycle regulators was detected by qRT-PCR. **F.** Western blotting was conducted to detect the protein levels of CDK4, cyclin D, and cyclin E in A498 and 786-O cells following transfection of si-DUXAP10. qRT-PCR data were expressed as fold change ($2^{-\Delta\Delta CT}$) and were evaluated after normalization to GAPDH levels in the same samples. β-actin protein was used as an internal protein control. $^{*}p < 0.05$, $^{**}p < 0.01$.

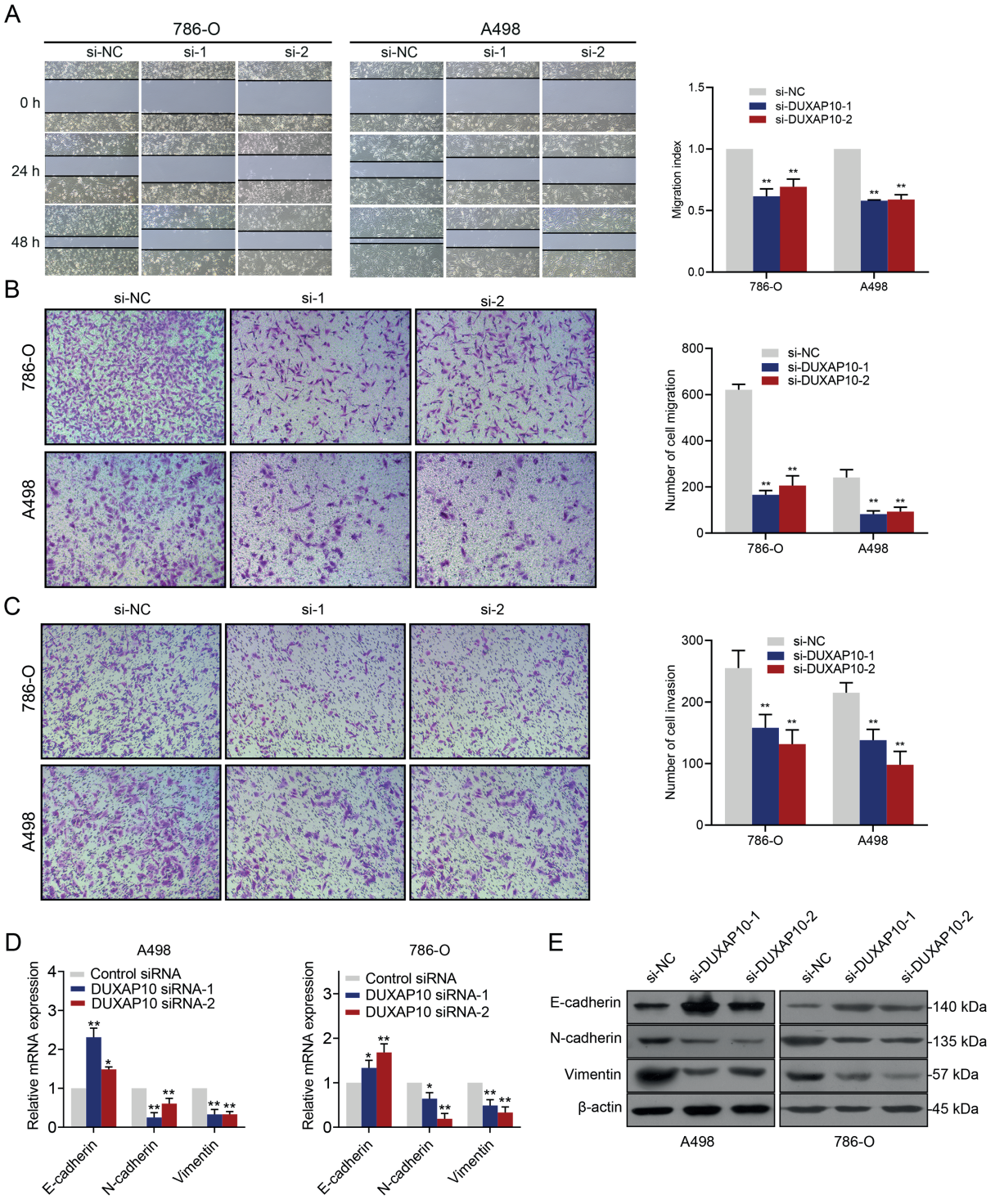

Figure 4. Decreased DUXAP10 expression inhibits the migration and invasion of RCC. **A**, Wound healing assays were conducted to investigate the migratory capacity of A498 and 786-o cells, 40X. **B-C**, The effects of DUXAP10 silencing on cell migration and invasiveness in RCC cells were evaluated by phase contrast microscope, 100X. **D,** The expression of EMT-related markers in RCC cells was verified by qRT-PCR. **E,** The expression of E-cadherin, N-cadherin, and vimentin in RCC cells was evaluated by western blotting. qRT-PCR data were expressed as fold change ($2^{-\Delta\Delta CT}$) and were evaluated after normalization to GAPDH levels in the same samples. β-actin protein was used as an internal protein control. $^{*}p < 0.05$, $^{**}p < 0.01$.

adults worldwide[17]. RCC has the highest mortality rate among urinary cancers[18]. If detected in the early stage, RCC is curable by nephrectomy, and this is partly due to a higher proportion of low-stage RCC identified using advanced early detection techniques[19,20]. However, one third of patients with RCC exhibit metastases[21]. In this complicated clinical setting, developments in molecular biology and diagnostic methods are revolutionizing the approach to RCC[22]. lncRNAs have been discovered to act as specific regulators in numerous cancers, including RCC[23-25]. lncRNA *DUXAP10* is a newfound RNA. Increasing evidence has indicated that *DUXAP10* could be a predictor of early metastasis and poor patient survival. Wei et al[26] reported that *DUXAP10* promotes metastasis in human non-small cell lung cancer. Lian et al[27] found that *DUXAP10* induces cell proliferation, which suggests that upregulation of *DUXAP10* may act as a potential biomarker to diagnose colorectal carcinoma patients. Xu et al[28] reported that *DUXAP10* promotes cell proliferation and invasion in gastric cancer. Altogether, these findings provide new perspectives for the diagnosis and treatment of malignant cancers.

However, the possible role of *DUXAP10* in RCC remained uncertain. In this study, we showed for the first time that the expression of *DUXAP10* was greatly increased in RCC tissues and cell lines compared to normal tissues and the HKC cell line. Moreover, we found that high levels of *DUXAP10* in RCC patients were closely correlated with worse histological stage, TNM stage, and metastasis. Furthermore, our results from the Kaplan-Meier survival analysis suggest that *DUXAP10* levels were correlated with poor prognosis of RCC patients. These observations indicated that *DUXAP10* might function as a novel diagnostic and prognosis biomarker in RCC.

Next, we employed a series of *in vitro* assays, including CCK-8 cell proliferation, migration, invasion, and colony formation assays, in the A498 and 786-O cell lines. These functional experiments indicated that knockdown of *DUXAP10* was able to inhibit cellular proliferation, induce cell cycle arrest in the G0/G1 phase, stimulate apoptosis, and decrease migration and invasion of RCC cells. Our findings validated the oncogenic roles of *DUXAP10* in RCC, which suggest that knockdown of *DUXAP10* could be a new potential therapeutic target for RCC treatment.

Increasing evidence suggests that the primary obstacle in the treatment of malignant tumors is recurrence and metastasis[29]. Metastasis is a feature of malignant cancer and relies on EMT, which is essential during embryonic development, tissue regeneration, and wound healing[30]. In addition, EMT plays a fundamental role in various pathologic processes, including tumor initiation, progression, and therapeutic resistance[31]. Liang et al[32] reported that lncRNA *PTAF* promoted EMT and invasion-metastasis in serous ovarian cancer. Wu et al[33] found that lncRNA *NKILA* suppresses TGF-beta-induced epithelial-mesenchymal transition in breast cancer. However, it remains unreported how *DUXAP10* contributes to the regulation of tumor metastasis in RCC. In this study, qRT-PCR and western blotting assays were conducted to examine several regulators associated with EMT. Interestingly, our study showed that silencing of *DUXAP10* could inhibit the metastatic capacity of RCC cells partly by upregulation of E-cadherin and downregulation of N-cadherin and vimentin. Given that *DUXAP10*-silenced cells fail to maintain mesenchymal-like phenotype markers, such as N-cadherin and vimentin, and acquire epithelial markers such as E-cadherin, *DUXAP10* might strengthen distant metastasis in RCC by affecting EMT progression. Our data indicated *DUXAP10* might be a therapeutic target to prevent metastasis in RCC. However, further research is required to enlarge the size of the clinical sample and cohort study. Moreover, the associated mechanisms should be further enlightened in the future.

Conclusions

In summary, for the first time, we report that *DUXAP10* is highly upregulated in RCC and that DUXAP10 levels positively correlate with poor prognosis for RCC patients. *DUXAP10* may promote the proliferation and invasion of RCC cells partly by functioning as a metastasis enhancer. Better comprehending of *DUXAP10* molecular mechanisms in RCC will be accessible for the improvement of new diagnostic and therapeutic methods to fight against RCC.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgments

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