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Knockdown of lncRNA SNHG7 inhibited cell proliferation and migration in bladder cancer through activating Wnt/β-catenin pathway

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ABSTRACT

It is identified that long non-coding RNAs (lncRNAs) play important roles in tumorigenesis. LncRNA SNHG7 has been found to be an oncogene in varieties of tumors including bladder cancer. However, its potential regulatory mechanism in bladder cancer still remains unknown. In this study, we discovered that the expression levels of SNHG7 were significantly increased in bladder cancer tissues and cell lines. Patients with high expression level of SNHG7 suffered from poor prognosis. Additionally, knockdown of SNHG7 induced declined cell viability, proliferation as well as G0/G1 cell cycle arrest. Furthermore, we found that cell migratory ability was markedly reduced after silencing SNHG7. Next, we verified that knockdown of SNHG7 reduced the protein level of β-catenin and thus decreased the level of its downstream targets including c-myc, cyclin D1 and E-cadherin, implying that SNHG7 might impact bladder cancer via Wnt/β-catenin pathway. Subsequently, the rescue assays performed in SNHG7 silenced T24 cells by using activator of Wnt/β-catenin signaling elucidated that re-activation of this pathway partly restored the inhibitory effects of SNHG7 suppression on biological behaviors of T24 cells. Collectively, SNHG7 elicited carcinogenic functions in bladder cancer partially via activating Wnt/β-catenin signaling pathway, suggesting a potential target for the treatment and prognosis of bladder cancer.

1. Introduction

Bladder cancer (BC), ranking fourth among men and eighth among women in most prevalent diagnosed cancers, is one of the most familiar urologic malignancies all over the world [2,13]. Bladder cancer patients always suffer from poor prognosis, although they are surgically treated with radical cystectomy (RC), radiation therapy, and postoperative instillation of chemotherapy or immunotherapy [22,25]. Because of high recurrence and mortality rate, it is urgent to discover novel molecular biomarkers for the treatment of bladder cancer.

Long non-coding RNAs (lncRNAs) is a kind of endogenous RNAs with a length of more than 200 nt but without meaningful open reading frames (ORFs) [7]. For this reason, lncRNAs is unable to code proteins but regulate the expression of genes instead [7,31]. Recently, growing evidence has proved that lncRNAs are involved in tumorigenesis and development of multiple human cancers [1,3,27,28]. Furthermore, it has been certified that lncRNAs may be potential therapeutic targets and biomarkers for diagnosis and prognosis in many cancers [8,10,12,15], even in bladder cancer [5,14,17,34].

Long non-coding RNA small nucleolar RNA host gene 7 (SNHG7) is a newly recognized oncogene that locates on chromosome 9 [32], and its dysregulation has been found to be associated with the progression of several cancers, such as gastric cancer, lung cancer, esophageal cancer, glioblastoma and prostate cancer [21,23,29,30,32,33]. Recently, SNHG7 has also been found to regulate proliferation, apoptosis and invasion of bladder cancer cells [36]. Nevertheless, the underlying modulatory mechanism by which SNHG7 aggravates bladder cancer progression need to be further studied.

The Wnt signaling pathway is an evolutionarily conserved pathway which has been reported to play an important role in embryonic development, and the dysregulation of this pathway contributes to tumor initiation and progression of various human cancers [4,11,19]. The Wnt/β-catenin signaling pathway, namely the canonical Wnt signaling pathway, begins with the unphosphorylated β-catenin translocated into the nucleus. In nucleus, β-catenin binds with transcription factors (TCF or LEF) and then activates downstream target genes, such as C-MYC, CCND1 and BIRC5, finally modulating cell proliferation, differentiation and survival [19]. Besides, Wnt/β-catenin signaling pathway has been

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identified to play a crucial role in bladder cancer [18]. Furthermore, SNHG7 has been reported to activate this pathway in glioblastoma [24]. However, whether SNHG7 modulates this pathway in bladder cancer remains unclear.

In the present study, we researched the expression and biological effect of SNHG7 in bladder cancer using tissues from patients with bladder cancer and cells lines. Moreover, the possible molecular mechanism underlying the regulation of SNHG7 on bladder cancer was also investigated in this study.

2. Materials and methods

2.1. Clinical samples

Total of 92 paired samples (bladder cancer tissues and adjacent non-cancerous tissues) were gathered from the Department of Urology, the Affiliated Hospital of Guilin Medical University. All of these samples were frozen stored at - 80 ℃ immediately after collecting. And the clinical and pathological features of every patient were collected as well. Each patient was well informed about that the samples would be used in future and then signed the informed consent. All patients involved in this study received no treatment prior to surgery. And the Ethics Committee of Guilin Medical University approved this study.

2.2. Cell lines and culture

Normal human bladder epithelial cell line SV-HUC-1 and six bladder cancer cell lines T24, 5637, 253 J, TCC, J82 and EJ cells were obtained from the Chinese Academy of Sciences (Shanghai, China). SV-HUC-1 cells were grown in F12 K medium with 10% fetal bovine serum (FBS). The 5637 cells and SW780 cells were cultured in RPMI-1640 Medium (Invitrogen) plus 1% antibiotics and 10% FBS. The other cells including T24 cell line were cultured in DMEM (Invitrogen) plus 1% antibiotics and 10% FBS. All cell lines were maintained at 37 ℃ with a humidified atmosphere with 5% CO_2 in an incubator. Medium was renewed every other day, except where otherwise demonstrated.

2.3. Interfering RNA transfection

T24 and 5637 cell lines with high SNHG7 expression were utilized for following experiments in vitro. The cells were transfected with particular shRNA targeting SNHG7 or corresponding empty vector (shCtrl; negative control) under the use of Lipofectamine 2000 transfection reagent according to the manufacturer's specification (Invitrogen, Carlsbad, CA, USA).

2.4. Real-time quantification PCR (RT-qPCR)

Total RNAs from tissues and cells were extracted by TRIzol reagent (Invitrogen Life Technologies) according to the manufacturer's instructions. Reverse transcription was carried out using PrimeScript RT reagent kit (Takara Bio, Inc., Otsu, Japan) under the manufacturer's instructions. RT-qPCR was conducted with SYBR Prime Script RT-PCR kits (Takara Bio, Inc.) on the basis of the manufacturer's instructions. GAPDH was acted as an endogenous control. The SNHG7 level was evaluated by using the $2^{-\Delta\Delta Ct}$ method. The PCR primers were as the following: GAPDH: 5′-GTCAGCCGCATCTTCTTTTG-3′ (sense) and 5′-GCGCCCAATACGACCAAATC-3′ (antisense). SNHG7: 5′-GTTGGGGT GTTGGCATTCTTGTT-3′ (sense) and 5′-TGGTCAGCCTGGTCACTC TGG-3′ (antisense).

2.5. MTT assay

MTT assay was used to test cell growth and viability of BC cells. First, cells with a density of 1×10^5 /well were cultured in a 96-well plates. After that, 20 μl of MTT stock solution (Sigma; 5 mg/ml) was added into all wells and then the plates were incubated at 37℃. Four hours later, the medium was removed and dimethyl sulfoxide (DMSO; Sigma Aldrich, Munich, Germany) was added to dissolve formazan crystals. Then shake the mixture gently for 15 min and measure the absorbance at 490 nm applying a microplate reader (Bio-Tek Instruments; Winooski, VT, USA).

2.6. Colony formation assay

To estimate monolayer colony formation, all kinds of cells (800 cells per well) were placed into six-well plates and incubated for two weeks. Then we fixed cells by methanol and stained cells using 1% crystal violet. Formed colonies (> 50 cells per colony) were counted manually.

2.7. Cell cycle analysis

After incubation for 48 h, cells distributed in specific cell cycle phases was estimated by DNA content using flow cytometry. Then we stained cells with propidium iodide (PI) and analyzed them by flow cytometer FACSVerse (BD, NJ, USA) on the basis of the DNA content.

2.8. Transwell assay

A 24-well Transwell chamber equipped with 8 μm pores was utilized to estimate cell migration. Cells, with a density of 1×10^5 cells per well, were added into 100 μl serum-free medium and then planted to the upper chamber of the 24-well plate and the lower chamber was filled with 600 μl medium including 10% FBS. After cultured for 24 h at 37℃, we fixed the cells migrated into the lower membrane surface with 75% methanol and stained them with 0.5% crystal violet. After that, the number of cells was counted under microscope at ×100 magnification in five optional fields which located at the center and places round of the membrane.

2.9. Western blot

The proteins were segregated using 10% sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and then transferred to polyvinylidene difluoride (PVDF) membranes (Roche). The membrane was blocked with 5%-skim milk for 1 h, and then washed by TBST for three times. After that, the membranes were incubated with primary antibodies at 4℃ overnight. The primary antibodies were as below: anti-β-catenin (1:2000; BD Biosciences, San Jose, CA, USA), anti-Cyclin D1 (1:2000; Cell Signaling Technology, Inc.), anti-c-myc (1:1000; Cell Signaling Technology, Inc.), anti-E-cadherin (1:1000, Cell Signaling Technology, Inc.) and anti-GAPDH (1:1000, Abcam, MA, USA). And then incubation with HRP-conjugated secondary antibodies (Abcam, MA, USA) at room temperature for 2 h was followed. In the end, the ECL detection system (Pierce Biotechnology, Rockford, USA) was used to analyze the results under manufacturer's directions. All experiments were independently performed for three times.

2.10. Statistical analysis

All data in this study were shown as mean ± standard deviation (SD). Statistical analyses were performed by using GraphPad Prism 5 software. Student's *t*-test and one-way ANOVA were applied to test the significant differences between two groups or among multiple groups. The overall survival curve of patients with bladder cancer was determined by using Kaplan-Meier analysis and the log-rank test. The significance was assessed by p value, and it was regarded statistically significant when differences with $p < 0.05$.

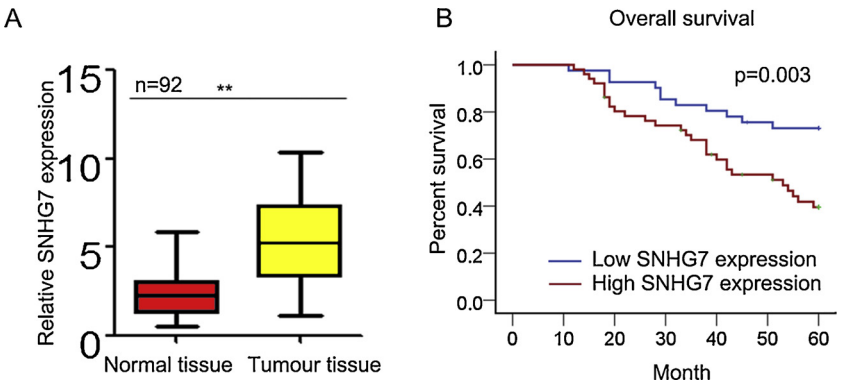

Fig. 1. The expression of SNHG7 was upregulated and correlated with poor overall survival (OS) in bladder cancer patients.
(A) SNHG7 expression in 92 paired BC tissues was evaluated by qRT-PCR. (B) Kaplan-Meier analysis and the log-rank test were employed to estimate the association between SNHG7 expression and overall survival in bladder cancer patients. *p < 0.05, **P < 0.01.

3. Results

3.1. The expression of SNHG7 was markedly upregulated in bladder cancer tissues and cell lines

Firstly, to find out the influences of SNHG7 on the progression of bladder cancer, we tested the expression of SNHG7 in bladder cancer tissues by RT-qPCR. As shown in Fig. 1A, the expression level of SNHG7 was obviously increased in BC tissues compared with the adjacent non-tumor tissues. In addition, bladder cancer patients who expressed high level of SNHG7 suffered from poor overall survival (OS) (Fig. 1B). Furthermore, we uncovered that SNHG7 expression was significantly higher in all six BC cell lines (T24, 5637, 253 J, TCC, J82 and EJ) in comparison with the normal human bladder epithelial cell line SV-HUC-1, among which T24 and 5637 cells showed higher SNHG7 level than any other detected cell lines (Fig. 2). All of these results implied that SNHG7 might be an oncogene in bladder cancer.

3.2. Expression of SNHG7 in BC patients was of important clinical significance

To further understand the effect of SNHG7 on bladder cancer, we next studied the relationship between SNHG7 expression and clinical pathological characteristics. As illustrated in Table 1, SNHG7 expression was strongly associated with tumor range (P = 0.029), lymph nodes (P = 0.043) and pathological stage (P = 0.002) rather than gender, smoking, age and metastasis. Besides, the Cox regression analysis determined that SNHG7 expression could be an independent marker for the prognosis of BC patients, so were several other parameters such as tumor range, metastasis, lymph nodes, and pathological stage (Table 2). Together, these data indicated that SNHG7 could be a prognostic biomarker for BC patients.

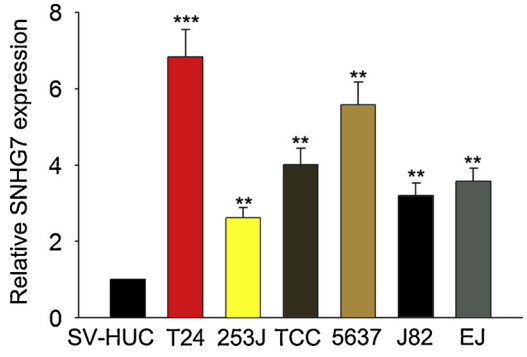

Fig. 2. SNHG7 expression in bladder cell lines and normal human bladder epithelial cells.
The mRNA levels of SNHG7 expression in all of the cells were tested by qRT-PCR. SNHG7 was expressed highly in bladder cancer cell lines compared with that in normal human bladder epithelial cells (SV-HUC-1), and its expression in T24 and 5637 cells were higher than other cancer cell lines. *p < 0.05, **P < 0.01.

Table 1
Correlation between lnc-SNHG7 Expression and Clinical Features. (n = 92).

Variable	Lnc-SNHG7 Expression		P-value
	low	high	
Age			
< 60	26	35	0.061
≥60	15	16	
Gender			
Male	31	41	0.831
Female	10	10	
Smoking			
No smoking	7	6	0.887
Smoking	34	45	
Tumor Range			
T1-T3	23	15	0.029
≥T4	18	36	
Metastasis			
negative	30	24	0.455
positive	11	27	
Lymph Nodes			
negative	33	25	0.043
positive	8	26	
Pathological Stage			
< IV	20	6	0.002
≥IV	21	45	

Low/high by the sample median. Pearson χ^2 test. P < 0.05 was considered statistically significant.

3.3. Knockdown of SNHG7 reduced BC cell survival and proliferation

To research the functional role of SNHG7 in human BC, loss-of-function assays were conducted in T24 and 5637 cells with high SNHG7 expression. Firstly, we found that SNHG7 was silenced in above two cells under shSNHG7 transfection compared to the negative control (shCtrl) group and mock (blank control) (Fig. 3A). Subsequently, the MTT assay indicated that knockdown of SNHG7 in T24 and 5637 cells led to a worse cell survival in contrast with controls (Fig. 3B). In addition, the results of colony formation assay elucidated that the number of colonies was significantly decreased in two BC cell lines after silencing SNHG7 while that in shCtrl groups changed little compared to mock (Fig. 3C). These data suggested that silencing SNHG7 inhibited cell survival and proliferation in BC cells.

Table 2
Multivariate analysis of prognostic parameters inpatients with bladder cancer by Cox regression analysis.

Variable	Category	P-value
Age	< 60 ≥60	0.660
Gender	Male Female	0.618
Smoking	No smoking Smoking	0.553
Tumor Range	T1-T3 ≥T4	0.012*
Metastasis	negative positive	0.019*
Lymph Nodes	negative positive	0.002*
Pathological Stage	< IV ≥IV	0.000*
Lnc-SNHG7 expression	Low High	0.000*

Proportional hazards method analysis showed a positive, independent prognostic importance of lncSNHG7 expression ($P < 0.001$), in addition to the independent prognostic impact of Pathological Stage ($P < 0.001$), Lymph Nodes ($P = 0.002$), Metastasis ($P = 0.019$), Tumor Range ($P = 0.012$). $P < 0.05$ was considered statistically significant.

3.4. Knockdown of SNHG7 induced G0/G1 cell cycle arrest and repressed cell migration in T24 and 5637 cells

To make clear the inhibitive effects of shSNHG7 on cell proliferation, flow cytometry analysis was used to determine the cell cycle distribution in T24 and 5637 cells. The percentage of cells in G0/G1 phase was increased while that in S phase and G2/M phase decreased after silencing SNHG7 in T24 and 5637 cells, demonstrating that knockdown of SNHG7 inhibited BC cell proliferation by inducing G0/G1 cell cycle arrest in T24 and 5637 cells (Fig. 4A). In addition, the impact of SNHG7 knockdown on cell migration capacity in these two BC cells was also assessed using transwell assay. As uncovered in Fig. 4B, both in T24 and 5637 cells, cell migration was notably suppressed in shSNHG7 transfected group compared with two control groups. Taken together, these findings demonstrated that SNHG7 played a promotive role in BC cell proliferation and migration.

3.5. SNHG7 promoted bladder cancer via Wnt/β-catenin pathway

Wnt/β-catenin signaling pathway has been identified to play a crucial role in a number of human cancers, including bladder cancer [18]. Thus, we hypothesized that SNHG7 affected the progression of bladder cancer via Wnt/β-catenin signaling pathway. First, we detected whether SNHG7 regulated the expression of the components of Wnt/β-catenin pathway using western blot analysis. As displayed in Fig. 5A, silenced SNHG7 obviously downregulated the protein level of β-catenin, cyclin D1, and c-myc but upregulated that of E-cadherin in T24 and 5637 cells, indicating that SNHG7 knockdown inactivated Wnt/β-catenin pathway in BC cells. Based on this, we next used LiCl to activate this pathway in SNHG7 silenced T24 cells to verify whether SNHG7 functioned in BC through this pathway. First of all, we found that LiCl didn't influence the expression of SNHG7 in T24 cells (Fig. 5B). Then the results of MTT and colony formation assay revealed that LiCl could reverse the reduction of cell proliferation ability caused by SNHG7 knockdown (Fig. 5C and D). Besides, the proportion of cells arrested at G0/G1 phase was evidently decreased after the treatment with LiCl (Fig. 5E). Furthermore, cell migration capacity presented a marked upregulation when activating Wnt/β-catenin pathway in SNHG7 silenced T24 cells (Fig. 5F). In sum, these observations revealed that SNHG7 exerted an oncogenic role in BC progression through activating Wnt/β-catenin signaling pathway.

4. Discussion

In the last decade, increasing evidence has identified that lncRNAs play important roles in the pathogenesis of various cancers. For example, Lv et al. reported that knockdown of lncRNA MNX1-AS1 inhibited cell proliferation and migration in ovarian cancer; Eoh et al. found that lncRNA SRA induced tumor proliferation and invasion through the NOTCH pathway in cervical cancer cell lines; and in 2018,

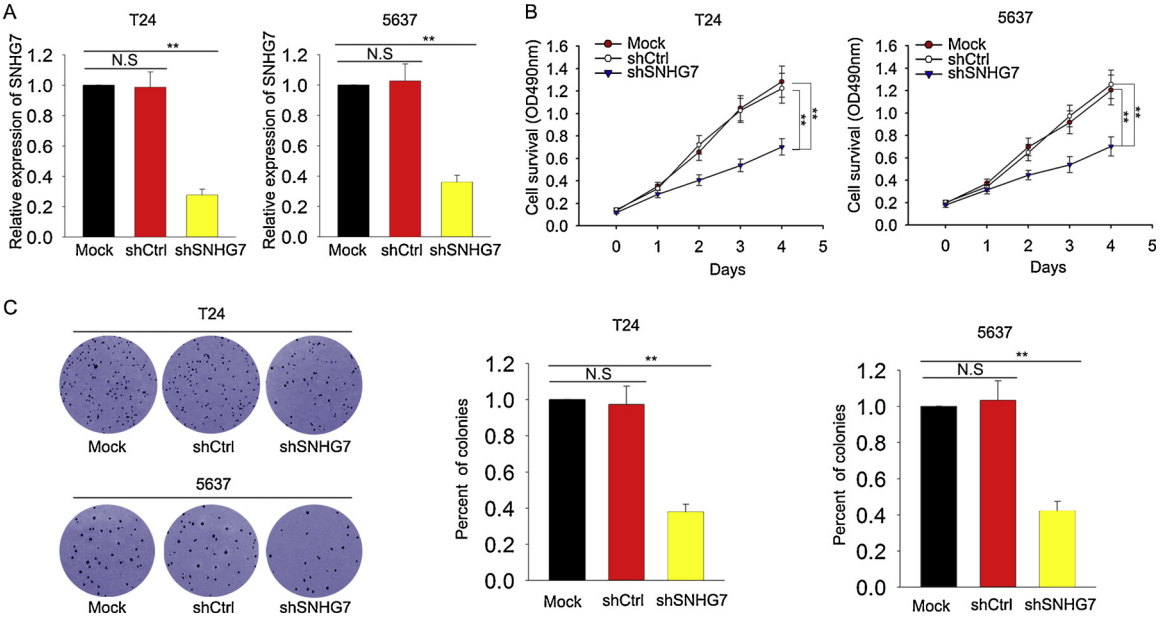

Fig. 3. Knockdown of SNHG7 inhibited cell survival and proliferation in T24 and 5637 cells.
(A) The transfection efficiency was evaluated by the reduction of SNHG7 expression tested using qRT-PCR. (B) MTT assay was carried out to examine the effect of SNHG7 on cell survival. Knockdown of SNHG7 led to a great diminishment of the rate of cell survivals. (C) Colony formation assay was utilized to explore the function of SNHG7 in cell proliferation ability. The number of formed colonies was largely reduced in si-SNHG7 group compared with other two groups in both T24 and 5637 cells. *$p < 0.05$, **$P < 0.01$.

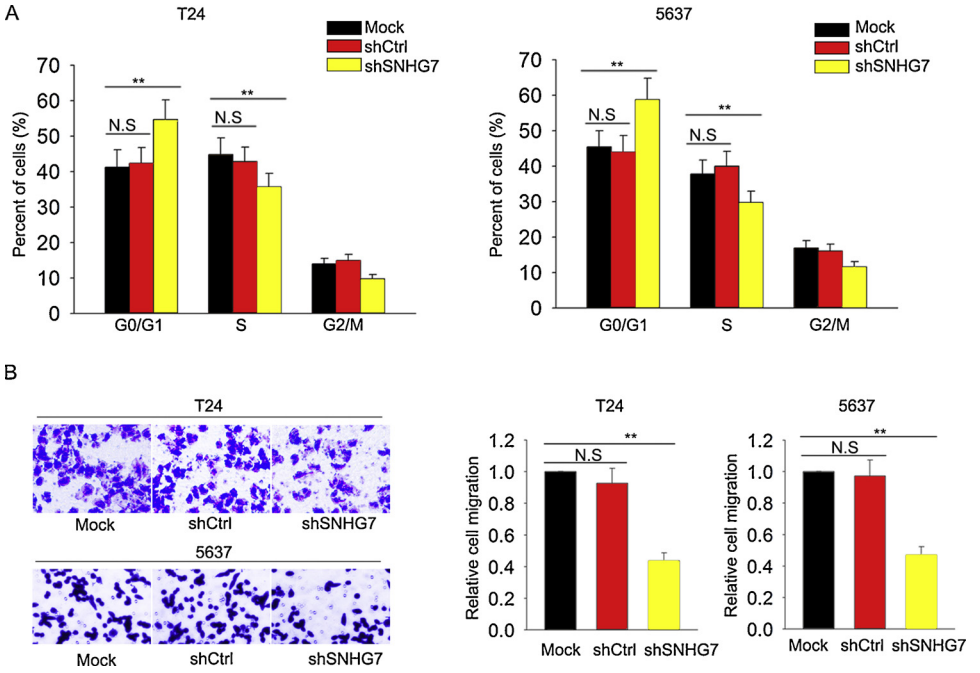

Fig. 4. Knockdown of SNHG7 arrested cell cycle at G0/G1 phase and suppressed cell migration in T24 and 5637 cells.
(A) Flow cytometry was applied to evaluate the distribution of cells in different cell cycle phases. In both of the two cells, the proportion of cells in G0/G1 phase was increased in shSNHG7group. (B) Transwell assay was applied to determine cell migration ability. The amount of migrated cells decreased largely when silencing SNHG7. *p < 0.05, **P < 0.01.

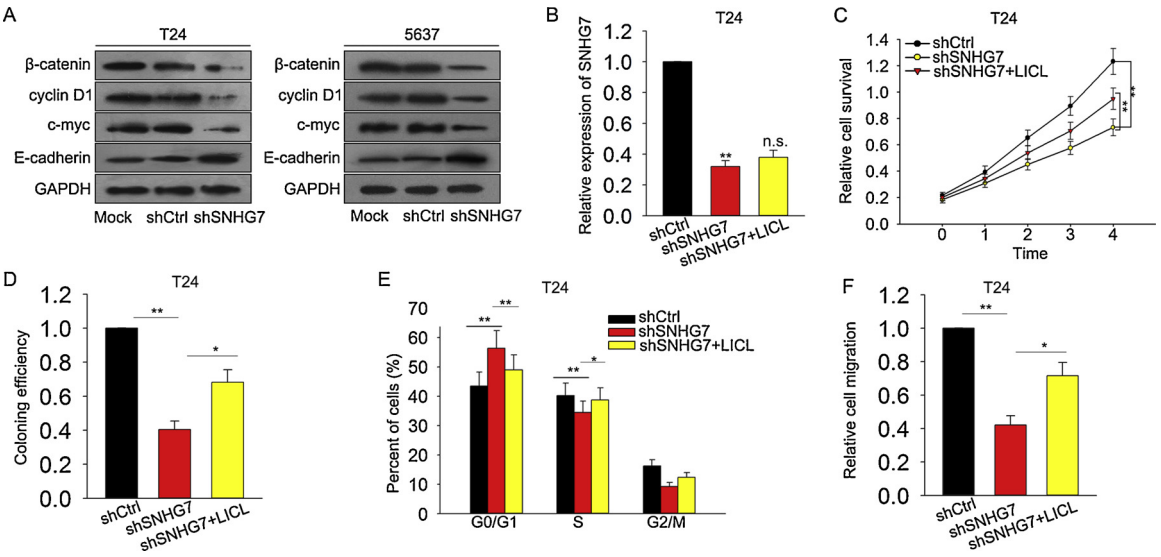

Fig. 5. SNHG7 promoted bladder cancer via Wnt/β-catenin pathway.
(A) The alterations of proteins involved in Wnt/β-catenin pathway were examined using western blot assay. (B) qRT-PCR results of SNHG7 expression after treating with LiCl in shSNHG7 transfected T24 cells. (C–D) The changes of cell proliferation ability were estimated by MTT and colony formation assay. (E) Flow cytometry analysis was applied to analyze the difference of cell cycle progression in T24 cells before and after LiCl treatment. (F) The alterations of cell migration capacity was detected by transwell assay. *p < 0.05, **P < 0.01.

Qi et al. declared that the long noncoding RNA lncRNA PARP1 promoted the progression of hepatocellular carcinoma through upregulation of PARP1 [6,16,20]. Recently, accumulating documents have revealed that lncRNAs also function in bladder cancer. Zhu et al. demonstrated that LSINCT5 interacting with NCYM promoted bladder cancer progression by activating Wnt/β-catenin signaling [37]. Zheng et al. explained that upregulated GAPLINC promoted tumor proliferation and invasion and predicted a poor prognosis in bladder cancer patients [35]. Even so, the effects of many other lncRNAs on bladder cancer still remain unknown.

SNHG7 is a potential oncogene which was newly identified in several cancers, such as gastric-cancer, lung cancer, esophageal cancer, glioblastoma and prostate cancer [21,23,29,30,32,33]. Besides, a recent report also uncovered that SNHG7 regulated BC cell proliferation, apoptosis and invasion [36]. Nevertheless, the underlying mechanisms by which SNHG7 functioned in bladder cancer are covered, and thus we conducted this study. Consistently, we also found that SNHG7 was highly expressed in BC tissues and cell lines, and its expression was closely related to clinical outcomes of patient with bladder cancer. Accordantly, we revealed that knockdown of SNHG7 inhibited cell proliferation and migration in BC cells, which was in line with the previous study [36]. In other words, we uncovered that SNHG7 predicted prognosis and promoted progression in bladder cancer.

Wnt/β-catenin pathway is one of the most frequent oncogenic signaling pathway which has been found to be dysregulated in a wide range of human cancers [26]. Some lncRNAs have been reported to dysregulate the Wnt/β-catenin signaling pathway in several cancers, including bladder cancer. For example, long non-coding RNA XIST

promotes cell growth and metastasis through regulating miR-139-5p mediated Wnt/β-catenin signaling pathway in bladder cancer [9]. Here, we found that SNHG7 could activate Wnt/β-catenin signaling in BC cells and confirmed that SNHG7 exerted its oncogenic function in BC via modulating the activation of Wnt/β-catenin signaling pathway.

In conclusion, this research elucidated that SNHG7 improved the progression of BC via activating Wnt/β-catenin pathway. Besides, all findings in the present study provided that SNHG7 could serve as a novel potential therapeutic target and prognostic biomarker for BC patients.

Conflict of interest

The authors declare that they have no conflict of interests.

Acknowledgements

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References

[1] C. Achour, F. Aguilo, Long non-coding RNA and Polycomb: an intricate partnership in cancer biology, Front. Biosci. 23 (2018) 2106.
[2] S. Antoni, J. Ferlay, I. Soerjomataram, A. Znaor, A. Jemal, F. Bray, Bladder Cancer incidence and mortality: a global overview and recent trends, Eur. Urol. 71 (2017) 96–108.
[3] J.J. Chan, Y. Tay, R.N.A. Noncoding, RNA regulatory networks in Cancer, Int. J. Mol. Sci. 19 (2018) 1310.
[4] H. Clevers, R. Nusse, Wnt/ β-catenin signaling and disease, Cell 149 (2012) 1192–1205.
[5] L. Du, W. Duan, X. Jiang, L. Zhao, J. Li, R. Wang, S. Yan, Y. Xie, K. Yan, Q. Wang, L. Wang, Y. Yang, C. Wang, Cell-free lncRNA expression signatures in urine serve as novel non-invasive biomarkers for diagnosis and recurrence prediction of bladder cancer, J. Cell. Mol. Med. 22 (2018) 2838–2845.
[6] K.J. Eoh, J. Paek, S.W. Kim, H.J. Kim, H.Y. Lee, S.K. Lee, Y.T. Kim, Long non-coding RNA, steroid receptor RNA activator (SRA), induces tumor proliferation and invasion through the NOTCH pathway in cervical cancer cell lines, Oncol. Rep. 38 (2017) 3481–3488.
[7] A. Fatica, I. Bozzoni, Long non-coding RNAs: new players in cell differentiation and development, Nat. Rev. Genet. 15 (2013) 7.
[8] H.-T. He, M. Xu, Y. Kuang, X.-Y. Han, M.-Q. Wang, Q. Yang, Biomarker and competing endogenous RNA potential of tumor-specific long noncoding RNA in chromophobe renal cell carcinoma, Onco. Ther. 9 (2016) 6399–6406.
[9] Y. Hu, C. Deng, H. Zhang, J. Zhang, B. Peng, C. Hu, Long non-coding RNA XIST promotes cell growth and metastasis through regulating miR-139-5p mediated Wnt/β-catenin signaling pathway in bladder cancer, Oncotarget 8 (2017) 94554–94568.
[10] J. Huang, T. Liu, C. Shang, Y. Zhao, W. Wang, Y. Liang, L. Guo, S. Yao, Identification of lncRNAs by microarray analysis reveals the potential role of lncRNAs in cervical cancer pathogenesis, Oncol. Lett. 15 (2018) 5584–5592.
[11] A. Klaus, W. Birchmeier, Wnt signalling and its impact on development and cancer, Nat. Rev. Cancer 8 (2008) 387.
[12] A.H. Li, H.H. Zhang, Overexpression of lncRNA MNX1-AS1 is associated with poor clinical outcome in epithelial ovarian cancer, Eur. Rev. Med. Pharmacol. Sci. 21 (2017) 5618–5623.
[13] H.-T. Li, C.E. Duymich, D.J. Weisenberger, G. Liang, Genetic and epigenetic alterations in bladder Cancer, Int. Neurourol. J. 20 (2016) S84–S94.
[14] Q. Li, C. Li, J. Chen, P. Liu, Y. Cui, X. Zhou, H. Li, X. Zu, High expression of long noncoding RNA NORAD indicates a poor prognosis and promotes clinical progression and metastasis in bladder cancer, Urol. Oncol.: Semin. Orig. Invest. 36 (2018) 310 e315-310.e322.
[15] C. Liang, J. Liu, H. Ge, Y. Xu, G. Li, J. Wu, The clinicopathological and prognostic value of long non-coding RNA ZEB1-AS1 in solid tumors: a meta-analysis, Clin. Chim. Acta (2018).
[16] Y. Lv, H. Li, F. Li, P. Liu, X. Zhao, Long noncoding RNA MNX1-AS1 knockdown inhibits cell proliferation and migration in ovarian Cancer, Cancer Biother. Radiopharm. 32 (2017) 91.
[17] Z. Ma, S. Xue, B. Zeng, D. Qiu, lncRNA SNHG5 is associated with poor prognosis of bladder cancer and promotes bladder cancer cell proliferation through targeting p27, Oncol. Lett. 15 (2018) 1924–1930.
[18] X.W. Mao, J.Q. Xiao, Z.Y. Li, Y.C. Zheng, N. Zhang, Effects of microRNA-135a on the epithelial-mesenchymal transition, migration and invasion of bladder cancer cells by targeting GSK3β through the Wnt/β-catenin signaling pathway, Exp. Mol. Med. 50 (2018) e429.
[19] P. Polakis, Wnt signaling and cancer, Genes Dev. 14 (2000) 1837–1851.
[20] H. Qi, Y. Lu, J. Lv, H. Wu, J. Lu, C. Zhang, S. Zhang, Q. Bao, X. Zhang, C. Xie, Z. Yin, The long noncoding RNA lncPARP1 contributes to progression of hepatocellular carcinoma through up-regulation of PARP1, Biosci. Rep. 38 (2018) BSR20180703.
[21] H. Qi, B. Wen, Q. Wu, W. Cheng, J. Lou, J. Wei, J. Huang, X. Yao, G. Weng, Long noncoding RNA SNHG7 accelerates prostate cancer proliferation and cycle progression through cyclin D1 by sponging miR-503, Biomed. Pharmacother. 102 (2018) 326.
[22] M. Racioppi, D. D'Agostino, A. Totaro, F. Pinto, E. Sacco, A. D'Addessi, F. Marangi, G. Palermo, P.F. Bassi, Value of current chemotherapy and surgery in advanced and metastatic bladder Cancer, Urol. Int. 88 (2012) 249–258.
[23] J. Ren, Y. Yang, J. Xue, Z. Xi, L. Hu, S.J. Pan, Q. Sun, Long noncoding RNA SNHG7 promotes the progression and growth of glioblastoma via inhibition of miR-5095, Biochem. Biophys. Res. Commun. 496 (2018).
[24] J. Ren, Y. Yang, J. Xue, Z. Xi, L. Hu, S.J. Pan, Q. Sun, Long noncoding RNA SNHG7 promotes the progression and growth of glioblastoma via inhibition of miR-5095, Biochem. Biophys. Res. Commun. 496 (2018) 712–718.
[25] T.L. Rose, M.I. Milowsky, Improving systemic chemotherapy for bladder Cancer, Curr. Oncol. Rep. 18 (2016) 27.
[26] F. Sanchez-Vega, M. Mina, J. Armenia, W.K. Chatila, A. Luna, et al., Oncogenic signaling pathways in the Cancer genome atlas, Cell 173 (2018) 321–337 e310.
[27] A. Sanchez Calle, Y. Kawamura, Y. Yamamoto, F. Takeshita, T. Ochiya, Emerging roles of long non-coding RNA in cancer, Cancer Sci. 109 (2018) 2093–2100.
[28] Y. Sánchez, M. Huarte, Long non-coding RNAs: challenges for diagnosis and therapies, Nucleic Acid Ther. 23 (2013) 15–20.
[29] K. She, J. Huang, H. Zhou, T. Huang, G. Chen, J. He, lncRNA-SNHG7 promotes the proliferation, migration and invasion and inhibits apoptosis of lung cancer cells by enhancing the FAIM2 expression, Oncol. Rep. 36 (2016) 2673.
[30] K. She, H. Yan, J. Huang, H. Zhou, J. He, miR-193b availability is antagonized by LncRNA-SNHG7 for FAIM2-induced tumour progression in non-small cell lung cancer, Cell Prolif. 51 (2017).
[31] X. Shi, M. Sun, H. Liu, Y. Yao, Y. Song, Long non-coding RNAs: a new frontier in the study of human diseases, Cancer Lett. 339 (2013) 159–166.
[32] M.W. Wang, J. Liu, Q. Liu, Q.H. Xu, T.F. Li, S. Jin, T.S. Xia, LncRNA SNHG7 promotes the proliferation and inhibits apoptosis of gastric cancer cells by repressing the P15 and P16 expression, Eur. Rev. Med. Pharmacol. Sci. 21 (2017) 4613–4622.
[33] L.J. Xu, X.J. Yu, B. Wei, H.X. Hui, Y. Sun, J. Dai, X.F. Chen, LncRNA SNHG7 promotes the proliferation of esophageal cancer cells and inhibits its apoptosis, Eur. Rev. Med. Pharmacol. Sci. 22 (2018) 2653.
[34] H. Yang, G. Li, B. Cheng, R. Jiang, ZFAS1 functions as an oncogenic long non-coding RNA in bladder cancer, Biosci. Rep. 38 (2018) BSR20180475.
[35] Z. Zheng, D. Zhu, F. Zhao, J. Han, H. Chen, Y. Cai, W. Xie, Upregulated GAPLINC predicts a poor prognosis in bladder cancer patients and promotes tumor proliferation and invasion, Oncol. Lett. 15 (2018) 6770–6776.
[36] X. Zhong, Z. Long, S. Wu, M. Xiao, W. Hu, LncRNA-SNHG7 regulates proliferation, apoptosis and invasion of bladder cancer cells assurance guidelines, J. BUON 23 (2018) 776–781.
[37] X. Zhu, Y. Li, S. Zhao, S. Zhao, LSINCT5 activates Wnt/β-catenin signaling by interacting with NCYM to promote bladder cancer progression, Biochem. Biophys. Res. Commun. (2018).