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Original Article

Long non-coding RNA CYTOR regulates proliferation and metastasis of colon cancer cells through regulating miRNA-105/PTEN axis

Yi Zhang[1], Weidong Jin[1], Dandan Ma[2], Jun Cao[2], Tao Fu[2], Zhaolin Zhang[2], Yang Zhang[2]

[1]*Second Department of Hepatobiliary Surgery, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China;* [2]*Department of General Surgery, General Hospital of Central Theater Command of PLA, Wuhan 430071, Hubei, China*

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Abstract: Colon cancer is a common malignancy, and its incidence and mortality have been increasing in recent years. This study aims to explore the regulation of long non-coding RNA CYTOR on proliferation and metastasis of colon cancer cells through miRNA-105/PTEN axis. Real-time quantitative PCR (qRT-PCR) disclosed that expression of CYTOR was significantly decreased in colon cancer tissues, compared with that of adjacent normal tissues, while miRNA-105 was significantly increased. Correlation study found that CYTOR was negatively correlated with miR-105. The proliferation, migration, and invasion rates of the LoVo cells with highly expressed CYTOR were significantly slower. miR-105 mimic could suppress the decrease in proliferation, migration, and invasion rates of colon cancer cells caused by overexpression of CYTOR. Additionally, the proliferation, migration, and invasion rates of the LoVo cells in miR-105 inhibition group were significantly slower. The Starbase database predicted the targeting of miR-105 by CYTOR, and qRT-PCR and dual luciferase reporter gene method were used to verify the targeting relationship of CYTOR and miRNA-105/PTEN axis. In conclusion, CYTOR can inhibit the proliferation and metastasis of colon cancer cells through targeted inhibition of the miR-105/PTEN axis.

Keywords: Colon cancer, lncRNA-CYTOR, miR-105, PTEN, proliferation, metastasis

Introduction

Colon cancer is a common malignancy whose incidence and mortality have been increasing in recent years. According to Chinese cancer statistics in 2015, the incidence and mortality of colon cancer rank fifth among all cancers [1]. At present, the common treatmentS for colon cancer include surgery, radiation therapy, chemotherapy, immunotherapy, Chinese medicine, and gene therapy [2]. Studies on colon cancer-related genes can guide clinicians in predicting the occurrence and development of the disease, evaluating the therapeutic effect, and judging prognosis.

Long non-coding RNAs (lncRNAs) are non-protein-encoding transcripts widely found in mammalian genomes [3], and studies have confirmed that lncRNAs affect tumor cell proliferation, invasion, apoptosis, and metastasis [4, 5]. As a lncRNA, CYTOR has been confirmed to be abnormally expressed in non-small cell lung cancer, gallbladder cancer, liver cancer, and other cancers [6, 7]. MicroRNAs (MiRs) are a group of endogenous non-coding RNA molecules, about 22 nt in length. They play an important role in cell differentiation, metabolism, proliferation, and apoptosis. Studies have confirmed that disorder of miR-105 contributes to the development of cancer [8]. However, few studies have been conducted on the role and related mechanisms of CYTOR in development and progression of colon cancer through regulating the miRNA-105/PTEN axis.

This study investigated the expression characteristics of CYTOR and the miRNA-105/PTEN axis in colon cancer, in order to provide a new theoretical basis for the diagnosis and treatment of colon cancer.

Materials and methods

Specimen collection

Twenty-nine cases of colon cancer specimens and adjacent normal tissues excised in our hospital from 2018 to 2019 were collected. No patients received preoperative anti-tumor treatment before specimen collection. The collection and use of tissue samples of patients was approved by the ethics committee of our hospital. All specimen tissues were immediately stored in liquid nitrogen at -80°C after excision.

Cell culture

LoVo human colon cancer cells were purchased from the cell bank of Chinese Academy of Sciences. All cells were cultured in RPMI-1640 medium (YajiBio, Minhang, Shanghai, China) containing 10% fetal bovine serum (FBS, EXcell, Shanghai, China), 1% penicillin, and 1% streptomycin (Invitrogen, Shanghai, China), and placed in a 37°C and 5% CO_2 incubator. They were routinely cultured and passaged. The solution was changed every 3 days, and passaged until the cells were confluent over the bottom of the flask. Cells in the logarithmic growth phase were taken for experiments.

Cell transfection

The LoVo cells were rinsed clean with PBS buffer, repeated 3 times, trypsinized for 2 min, and transferred to a sterile 15 mL centrifuge tube. After that, they were centrifuged and counted, and seeded at 4×10^5 cells per well in 6-well plates. When the fusion rate was about 70%, the transfection reagent was diluted at a concentration of 3 μL/L with serum-free medium, and incubated at 37°C for 20 min. The CYTOR and the NC were diluted at a concentration of 50 μmol/L with serum-free medium, respectively, incubated at room temperature for 5 min, mixed with the same volume of the transfection reagent, and cultured in a 37°C incubator. After 12 hours, the state of the transfected cells was observed, and the serum-free medium was changed to complete medium. After 48 hours of further culture, the RNA was extracted to verify the transfection efficiency. miR-105 mimics, inhibitor, and the controls were transfected into the Lovo human colon cancer cells in the same manner. CYTOR knockout and overexpression plasmids were designed and integrated by GenePharma (Shanghai, China). The blank plasmid served as a control.

Gene knockout and overexpression

LoVo cells with CYTOR gene over-expression and miR-105 overexpression and inhibition were enforced by expression of the lentivirus of siRNA.

Real-time PCR

All RNA was extracted with TRIzol reagent (Invitrogen, Shanghai, China) according to the instructions. miR-105 was amplified with TaqMan miR-105 MicroRNA Kit (Applied Biosystems, Foster City, CA), and transformed into cDNA by SuperScript First Strand cDNA System (Invitrogen, Shanghai, China). qRT-PCR analysis was performed on ABI Step One real-time PCR system (Applied Biosystems) with SYBR Premix Ex Taq Kit (Takara, Dalian, China). The conditions for quantitative real-time polymerase chain reaction were: pre-denaturation at 95°C for 10 min, 95°C for 15 s, and 60°C for 15 s, for 45 cycles, and the fluorescence signal temperature was 60°C. GAPDH was used as the internal reference to detect the expression of CYTOR, and U6 to detect the expression of miR-105. The $2^{(-\Delta\Delta Ct)}$ method was used for statistical analysis. Each experiment was repeated and measured three times. CYTOR primer sequences: upstream primer 5'-AGAATGAAGGCTGAGGTGTG-3', downstream primer 5'-CAGCGACCATCCAGTCATTTA-3'; miR-105 primer sequences: upstream primer 5'-GCGTCTGGAATGTAAGGAAGTG-3', downstream primer 5'-GTGCAGGGTCCGAGGT-3'; PTEN primer sequences: upstream primer 5'-CAGATTATGGAATGTAGGCGGCTTGA-3', downstream primer 5'-TGGCAATAGCCGAACAGTTCT-3'; GAPDH primer sequences: upstream primer 5'-GAGTCAACGGATTTGGTCGT-3', downstream primer 5'-TTGATTTTGGAGGGATCTCG-3'; U6 primer sequences: upstream primer 5'-TTGGTCTGATCTGGCACATATAC-3', downstream primer 5'-AAAAATATGGAGCGCTTCACG-3'.

Western blot

Cancer cells after treatment were collected and RIPA (Roche, Shanghai, China) was added for protein lysate. Cells were fully lysed on ice

and underwent 15-min centrifugation at 14000 rpm in a low-temperature centrifuge to collect the total protein. Then, the 50 ug total protein went through a 2-hour electrophoresis with 12% polyacrylamide gel (SDS-PAGE) at 100 V. The separated proteins were electronically transferred to polyvinylidene fluoride (PVDF) membranes. Next, the membranes were sealed with 5% skim milk powder at room temperature for 1 h, washed with TBST for 3 times, 10 min each and incubated with primary antibodies E-cadherin (Abcam, ab1416, 1:1000, MA, USA), Vimentin (Abcam, ab92547, 1:1500), N-cadherin (Abcam, ab76057, 1:1000), PTEN (Abcam, ab32199, 1:1200), AKT (Abcam, ab8805, 1:1000), p-AKT (Abcam, ab38449, 1:1000), or GAPDH (Abcam, ab9484, 1:1000) overnight at 4°C. After washing the membranes in TBST, the membranes were incubated at room temperature with horseradish peroxidase (HRP)-labeled anti-rabbit secondary antibody (concentration 1:300) for 1 h. After washing membranes in TBST, Chemistar ECL Western Blotting Substrate (Invitrogen, Shanghai, China) was used to color the protein bands, and the gray values of each protein band were analyzed through Image J.

CCK-8 cell proliferation assay

CCK-8 was used to generate cell growth curves, and cells were harvested in log phase and digested with trypsin (0.25%). 10% FBS was used to prepare cell suspension to be placed in the medium, and LoVo cells (3,000 cells per well) were placed in 96-well plates and incubated for 1, 2, 3, and 4 days, respectively. Then, 10 μl of Enhanced Cell Counting Kit-8 (Beyotime, Beijing, China) was added and incubated at 37°C for 1 hour. The absorbance was measured at 450 nm. Each experiment was repeated and measured three times.

Transwell assay

After being dispersed with 0.25% trypsin, LoVo cells were centrifuged, resuspended, and dispersed in the single well of a 24-well culture plate. An artificial basement membrane chamber (8 μm pore size; Corning, Beijing, China) was used for invasion, but not for migration. 5×10^4 transfected cells were placed in the upper chamber, and Matrigel was added. 10% FBS medium was placed in the lower chamber, which was filled with 400 μL of RPMI-1640. After being incubated at 37°C for 24 hours, the cells that failed to migrate were removed from the upper chamber. The Transwell membrane was fixed with 4% paraformaldehyde for 10 minutes and stained with 0.5% crystal violet. After being rinsed off with tap water, they were counted under an inverted microscope. All experiments were repeated three times.

Dual luciferase reporter assay

A luciferase reporter assay was performed with the dual luciferase reporter system (Promega, Madison, WI, USA). The target fragments of wild-type CYTOR and mutant CYTOR were integrated into PGL3 receptor (Promega, Madison, WI, USA) to construct wild-type PGL3-CYTOR (CYTOR-WT), PTEN-WT, and mutant pGL3-CYTOR (CYTOR-MT), PTEN-MT. CYTOR-WT or CYTOR-MT was co-transfected into VoLo cells with miR-105 mimics or a negative control. After 48 hours of transfection, luciferase activity was determined according to the manufacturer's instructions. All experiments were repeated three times.

Statistical methods

SPSS software was used for data analysis. All data were represented by ($\bar{x} \pm s$). T-test was used for statistical analysis, and chi-square test was used to analyze the correlation between CYTOR and miRNA-105 expression. $P < 0.05$ was considered significant.

Results

Expression of CYTOR and miR-105 in colon cancer

Compared with that of adjacent tissues, CYTOR expression in colon cancer tissues was significantly down-regulated ($P<0.001$, **Figure 1A**); miR-105 expression was significantly up-regulated ($P<0.01$, **Figure 1B**); and there was a negative correlation between CYTOR and miR-105, ($P<0.05$, **Figure 1C**).

Up-regulation of CYTOR gene inhibits the proliferation and migration of colon cancer cells

RT-PCR demonstrated that CYTOR in the CYTOR over-expression group was increased ($P< 0.05$, **Figure 2A**). CCK-8 assay showed that

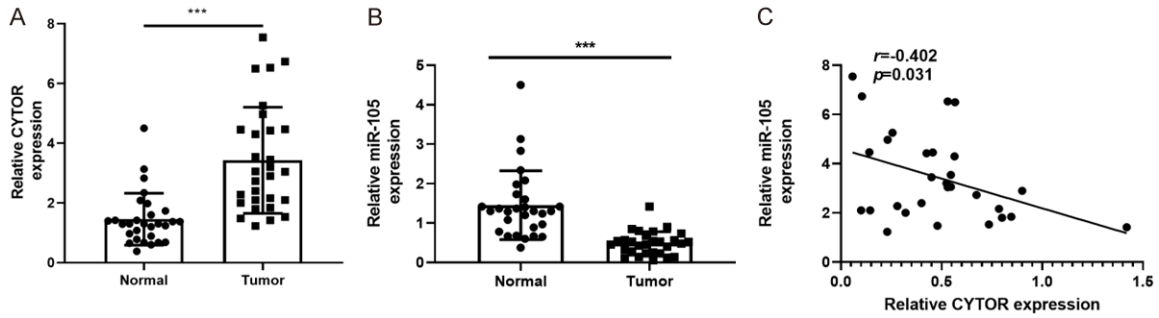


Figure 1. Expression of CYTOR and miR-105 in colon cancer and adjacent normal tissues detected by qRT-PCR. A: Expression characteristics of CYTOR in colon cancer and adjacent normal tissues; B: Expression characteristics of miR-105 in colon cancer and adjacent normal tissues; C: Correlation analysis of expression of CYTOR and miR-105 in colon cancer tissues. *P<0.05, **P<0.05, ***P<0.001.

the proliferation rate of LoVo cells with CYTOR over-expression was significantly slower than that of non-overexpressed cells (P<0.05, **Figure 2B**). Transwell cell migration test showed that CYTOR over-expression significantly reduced the migration (P<0.05, **Figure 2C**) and invasion (P<0.05, **Figure 2D**) of LoVo cells. WB results showed that CYTOR overexpression promoted the expression of E-cadherin, but inhibited the expression of vimentin and N-cadherin (P<0.05, **Figure 2E**). To explore the downstream mechanism, we found that CYTOR could inhibit the activation of Akt by promoting the expression of tumor suppressor gene PTEN (P<0.05, **Figure 2F**, **2G**). These results indicated that up-regulation of CYTOR could inhibit the proliferation and migration of colon cancer cells through increased PTEN.

Down-regulation of miR-105 could inhibit the proliferation and migration of colon cancer cells

RT-PCR demonstrated that miR-105 in the miR inhibition group was decreased (P<0.05, **Figure 3A**). CCK-8 assay showed that the proliferation rate of LoVo cells with miR-105 down-expression was significantly slower (P<0.05, **Figure 3B**). Transwell cell migration test showed that inhibition of miR-105 expression significantly reduced the migration (P<0.05, **Figure 3C**) and invasion (P<0.05, **Figure 3D**) of LoVo cells. WB results showed that inhibition of miR-105 expression promoted E-cadherin, but inhibited the expression of vimentin and N-cadherin (P< 0.05, **Figure 3E**). To explore the downstream mechanism, we found that miR-105 inhibition could inhibit the activation of Akt by promoting the expression of tumor suppressor gene PTEN (P<0.05, **Figure 3F**, **3G**). These results indicated that down-regulation of miR-105 could inhibit the proliferation and migration of colon cancer cells through increased PTEN.

CYTOR can act directly on miR-105

Possibletarget genes for CYTOR were searched in the Starbase database (www.starbase.sysu.edu.cn), and CYTOR was found to contain a conserved target site for miR-105. PTEN was found to contain a conserved target site for miR-105 (**Figure 4A**). The dual luciferase reporter assay was used to verify the direct binding of CYTOR to miR-105, and miR-105 to PTEN. The results showed that miR-105 mimic significantly reduced luciferase activity of CYTOR and PTEN luciferase reporter vector compare to the control (P<0.05, **Figure 4B**). After over-expression of CYTOR in LoVo cells, the expression of miR-105 was significantly decreased (P<0.05, **Figure 4C**), whereas up-regulation of miRNA had no significant effect on CYTOR expression (P>0.05, **Figure 4D**).

CYTOR regulates proliferation and migration of colon cancer cells by targeting miR-105

CCK-8 assay demonstrated that transfection of miR-105 mimics deduced LoVo cell proliferation, while CYTOR overexpression inhibited the phenomena of miR-105 mimics (**Figure 5A**). Transwell assays demonstrated that transfection of the miR-105 mimics increased the migration and invasion capacity of LoVo cells, which was offset by overexpression of CYTOR (**Figure 5B**, **5C**). WB results showed that miR-105 mimics inhibited E-cadherin, but promoted

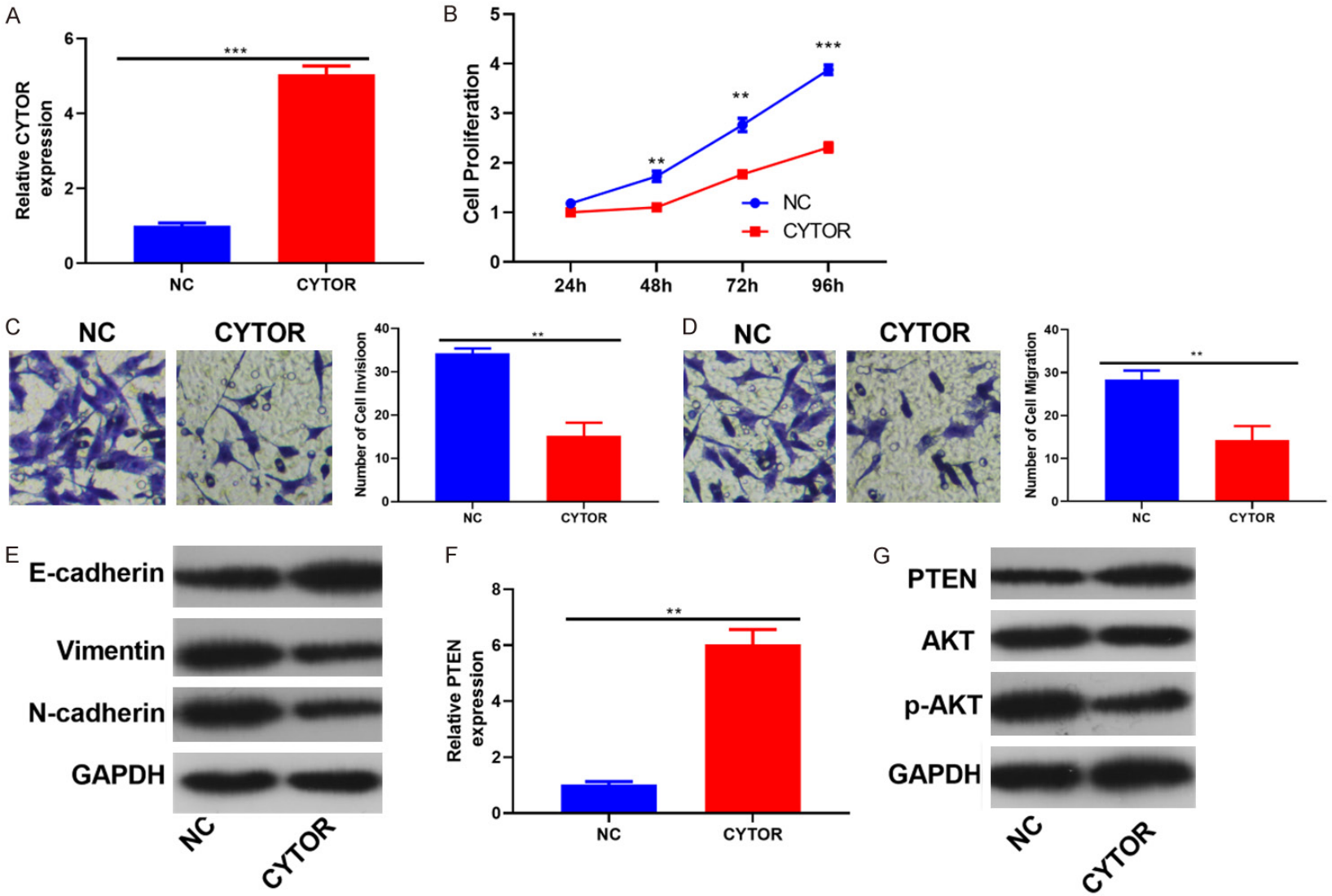


Figure 2. Effect of up-expressed CYTOR on the proliferation, migration, and invasion of LoVo colon cancer cells. (A) Expression of CYTOR was detected by RT-PCR; (B) Cell proliferation detected by CCK8; (C) Cell migration detected by Transwell assay; and (D) Cell invasion detected by Transwell assay; (E) EMT marker, E-cadherin, vimentin and N-cadherin were detected by WB; (F, G) RT-PCR (F) and WB (G) were used to detect PTEN and AKT in groups. *P<0.05, **P<0.05, ***P<0.001.

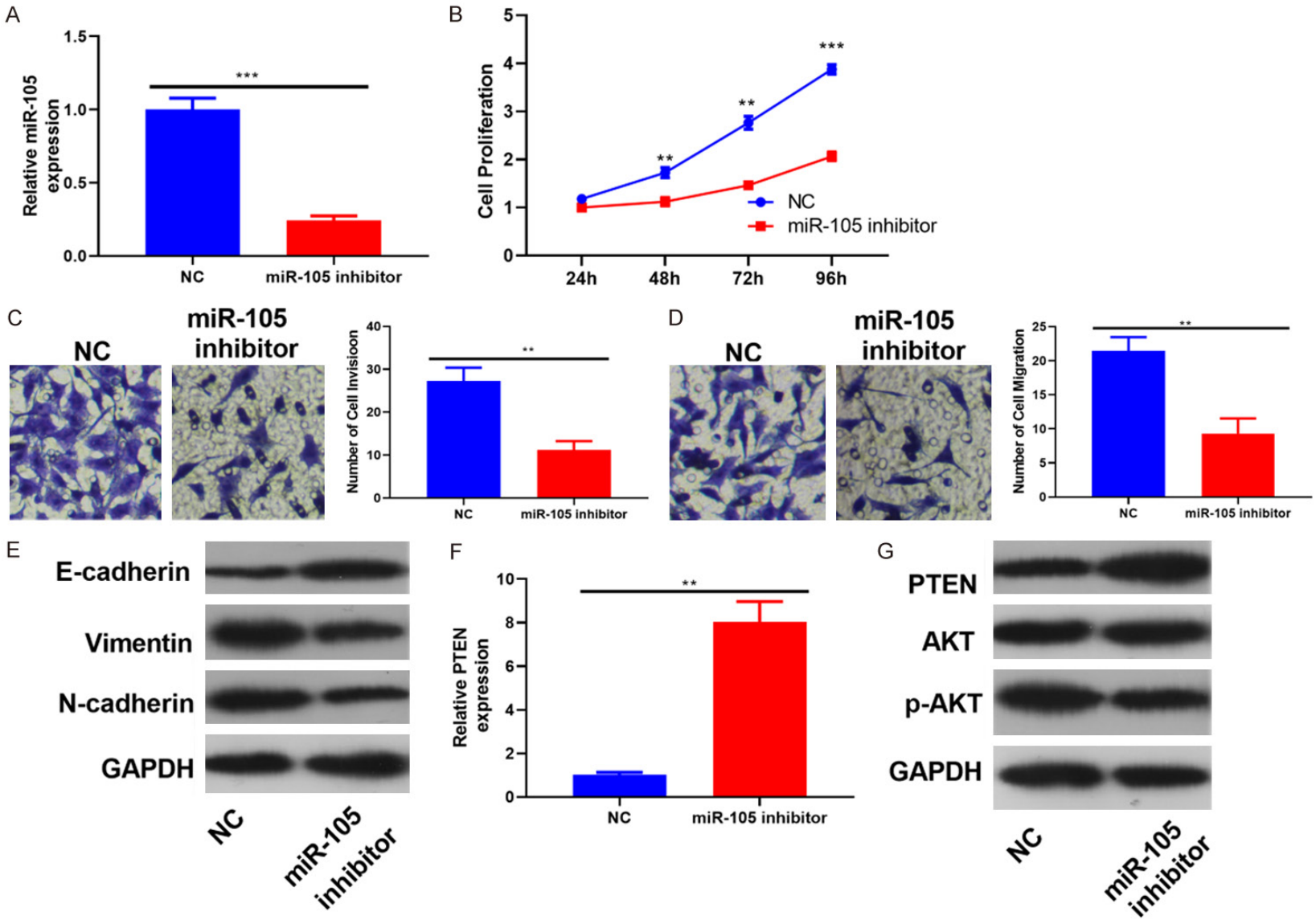


Figure 3. Effect of underexpressed miR-105 on the proliferation, migration, and invasion of LoVo colon cancer cell lines. (A) Expression of miR-105 was detected by RT-PCR; (B) Cell proliferation detected by CCK8; (C) Cell migration detected by Transwell assay; and (D) Cell invasion detected by Transwell assay; (E) EMT marker, E-cadherin, vimentin and N-cadherin were detected by WB; (F, G) RT-PCR (F) and WB (G) were used to detect PTEN and AKT in groups. *P<0.05, **P<0.05, ***P<0.001.

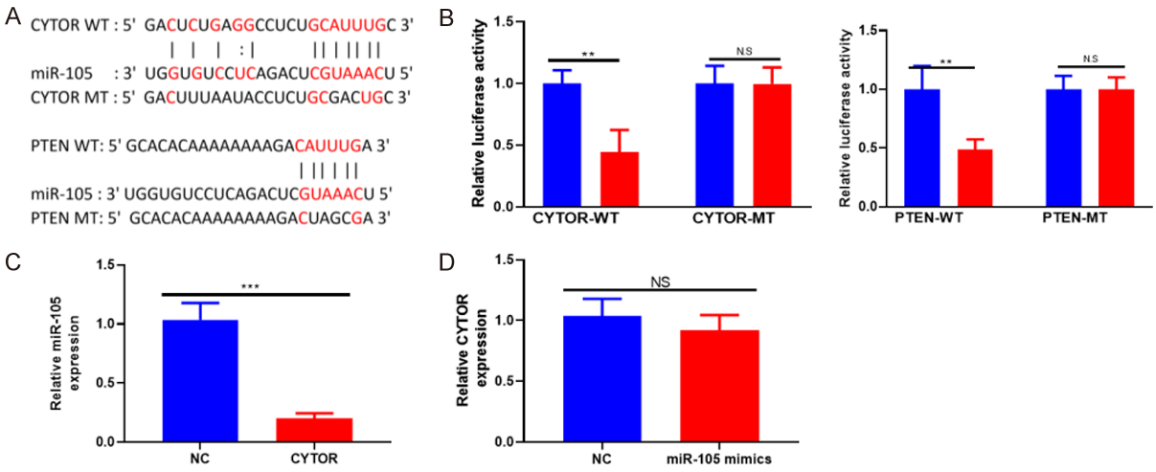


Figure 4. Expression characteristics and interactions of CYTOR and miR-105/PTEN in colon cancer tissues and cells. A: Starbase database (www.starbase.sysu.edu.cn) pairing relationship between CYTOR/miR-105/PTEN; B: Targeting relationship between miR-105 and CYTOR/PTEN by dual luciferase reporter assay; C, D: Relationship between expression of CYTOR and miR-105 in colon cancer cells. *P<0.05, **P<0.05, ***P<0.001.

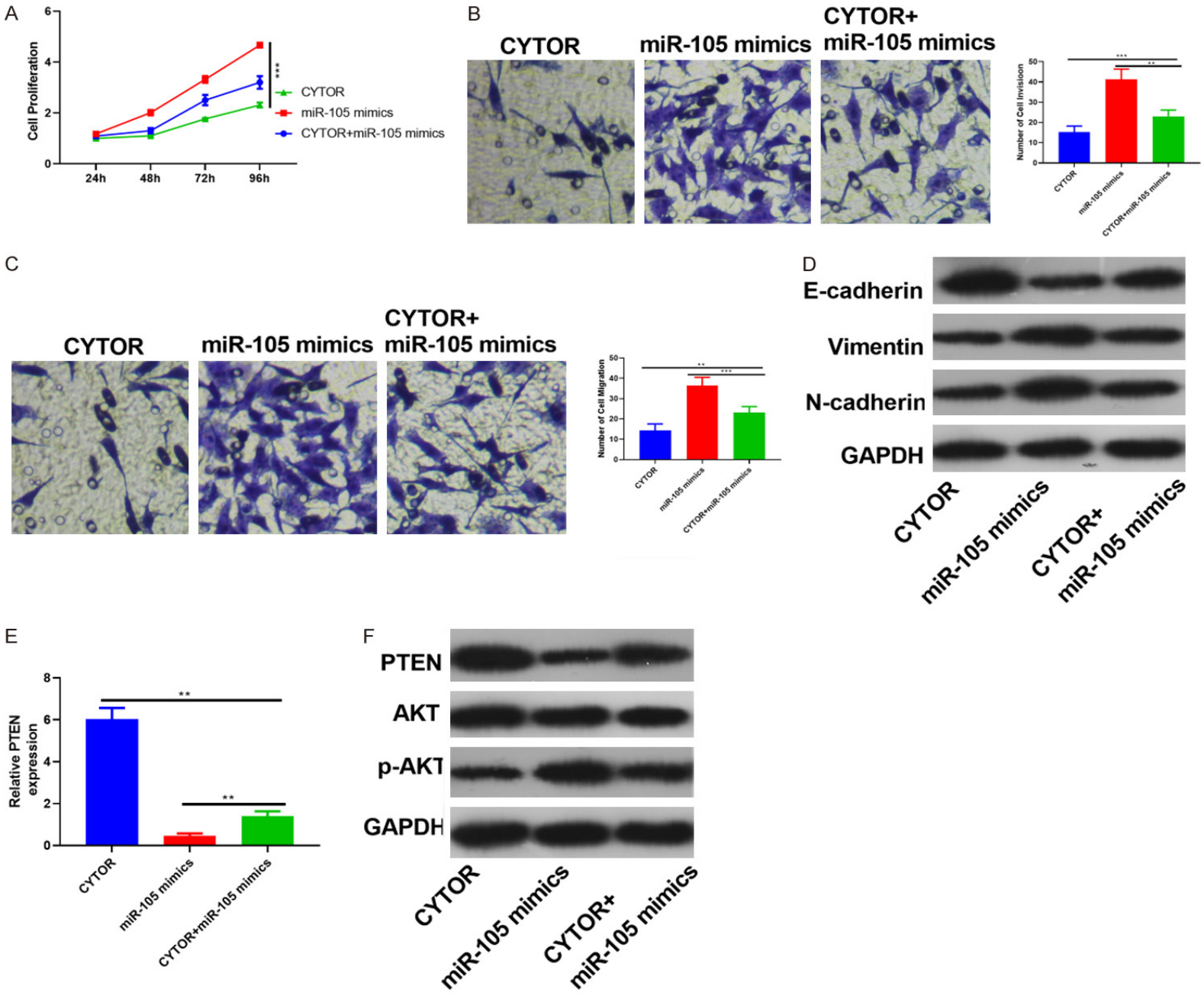
the expression of vimentin and N-cadherin, which was revised by overexpression of CYTOR (P<0.05, **Figure 5D**). To explore the downstream mechanism, we found that miR-105 mimics could activate Akt by inhibition the expression of tumor suppressor gene PTEN, and overexpression of CYTOR partially suppressed this phenomenon (P<0.05, **Figure 5E**, **5F**). These results suggested that CYTOR regulates proliferation and migration of colon cancer cells by targeting miR-105.

Discussion

The occurrence and development of colon cancer is a multi-step and long-term process in which multiple factors are involved. In recent years, studies have revealed that abnormal expression of lncRNA is not only closely related to colon cancer, but also can be used as a biologic indicator for diagnosis and therapeutic target of colon cancer [9]. From a mechanical point of view, lncRNAs are a non-coding RNAs in the nucleus and cytoplasm that regulate the expression level of genes in the form of RNA. Though lncRNAs are not able to encode proteins, they play a decisive role in protein expression [10]. Recently, studies have proven the important role of lncRNAs in the occurrence and development of tumor diseases [11]. lncRNAs exert their role through epigenetic, transcriptional, and post-transcriptional regulation [12]. Huang et al. [13] showed that lncRNA HOXB-AS3 could encode a peptide to inhibit the development of colon cancer. Xue et al. [14] found that lncRNA CYTOR promoted the progression of colorectal cancer by interacting with NCL and Sam68. Yue et al. [15] found that lncRNA CYTOR promoted metastasis of colon cancer through Wnt/β-catenin signaling.

CYTOR, a newly discovered lncRNA, has been proven to be a key regulator in the process of cancer development. Zhu et al. [16] found that CYTOR could promote proliferation and invasion of glioma cells by negatively regulating miR-4775, while lowly expressed CYTOR could inhibit the progression of glioma. Wang et al. [17] found that down-regulation of CYTOR expression could inhibit the progression of gastric cancer by regulating the miR-193b-3p/ETS1 axis. Zhang et al. [18] found that down-regulation of CYTOR suppressed the biologic activity of lung cancer through the EGFR/PI3K/AKT pathway. Unlike the previous report, this study found that CYTOR was down-expressed in colon cancer tissues compared to adjacent normal tissues, and highly expressed CYTOR could significantly inhibit proliferation, migration, and invasion of colon cancer cells, indicating that CYTOR plays a cancer-inhibiting effect in the progression of colon cancer. Due to the small number of cases in this study, and since only one cell line was selected, this may cause the difference from the previous results, but the reasons need to be further explored.

In addition, a large number of studies have revealed that lncRNAs can interfere with the


A
Cell Proliferation
24h
48h
72h
96h
CYTOR
miR-105 mimics
CYTOR+miR-105 mimics
B
CYTOR
miR-105 mimics
CYTOR+
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Number of Cell Invisioon
C
CYTOR
miR-105 mimics
CYTOR+
miR-105 mimics
Number of Cell Migration
D
E-cadherin
Vimentin
N-cadherin
GAPDH
CYTOR
miR-105 mimics
CYTOR+
miR-105 mimics
E
Relative PTEN expression
F
PTEN
AKT
p-AKT
GAPDH

Figure 5. Effect of CYTOR and miR-105 on the proliferation, migration and invasion of LoVo cells. (A) Cell proliferation detected by CCK8; (B, C) Cell migration and invasion were detected by Transwell assay; (D) EMT marker, E-cadherin, vimentin and N-cadherin were detected by WB; (E, F) RT-PCR (E) and WB (F) were used to detect PTEN and AKT in groups. *P<0.05, **P<0.05, ***P<0.001.

biologic functions of microRNAs through complementary base pairing, and the latter, also as one of the important factors in tumor formation and metastasis, has a certain influence on the biologic behavior of tumor cells when it is up- or down-regulated. In this study, we found through database analysis that CYTOR could inhibit function of miR-105 in a targeted manner. So, we detected the expression of miR-105 in colon carcinoma tissues. Interestingly, miR-105 expression was up-regulated, and there was a negative correlation between CYTOR and miR-105, suggesting that both CYTOR and miR-105 expression exert an effect on colon cancer. Down-regulation of miR-105 inhibited the progression and metastasis of colon cancer cells. These studies showed that miR-105 could promote the progression of colon cancer and was a miRNA with a tumor suppressor effect. miR-105, however, also exerts a tumor promoter effect in other tumors. For example, over-expression of miR-105 deduces resistance to Euthyrox by targeting MAP4K3 in papillary thyroid carcinoma [19]. miR-105 promotes proliferation and migration of esophageal cancer and acts as an oncogene, and inhibits apoptosis by regulating expression of cMET [20]. miR-105 down-regulation also suppresses the proliferation, migration, and invasion of non-small cell lung cancer cells by targeting the FHL1 gene and is sponged by Long Intergenic Noncoding RNA 00261 [21]. On this basis, we further explored the relationship between CYTOR and miR-105, and found that miR-105 expression was significantly upregulated when CYTOR had low expression in colon cancer cells, and cell proliferation, migration, and invasion abilities were significantly reduced after miR-105 mimics acted on the colon cancer cells with overexpressed CYTOR. It was confirmed that CYTOR could inhibit miR-105, and the limited function of miR-105 was likely to be an important mechanism in the development of colon cancer.

In sum, CYTOR can inhibit the proliferation and metastasis of colon cancer cells through regulation of miR-105, but the specific mechanism and the binding site remain to be determined by further studies. This study explores new mechanisms in the development of colon cancer and provides a novel theoretical basis for diagnosis and treatment.

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Disclosure of conflict of interest

None.

Address correspondence to: Yang Zhang, Department of General Surgery, General Hospital of Central Command of PLA, 627 Wuluo Road, Wuhan 430071, Hubei, China. Tel: +86-27-68878888; E-mail: zhangyang0012@sina.cn

References

[1] Hofseth Lorne J, Hebert James R, Chanda A and Chen H, Love B, Pena M, Murphy E, Sajish M, Sheth A, Buckhaults P and Berge F. Early-onset colorectal cancer: initial clues and current views. Nat Rev Gastroenterol Hepatol 2020; 17: 352-364.

[2] Robert L, Katie N, Shabnam S and Karin M. Immunotherapy, inflammation and colorectal cancer. Cells 2020; 9: 618.

[3] Li J, Meng H, Bai Y and Wang K. Regulation of lncRNA and its role in cancer metastasis. Oncol Res 2016; 23: 205-17.

[4] Wei GH and Wang X. LncRNA MEG3 inhibit proliferation and metastasis of gastric cancer through p53 signaling pathway. Eur Rev Med Pharmacol Sci 2017; 21: 3850-3856.

[5] She K, Huang J, Zhou H, Huang T, Chen G and He J. LncRNA-SNHG7 promotes the proliferation, migration and invasion and inhibits apoptosis of lung cancer cells by enhancing the FAIM2 expression. Oncol Rep 2016; 36: 2673-2680.

[6] Liang J, Wei X, Liu Z, Cao D, Tang Y, Zou Z, Zhou C and Lu Y. Long noncoding RNA CYTOR in cancer: a TCGA data review. Clinica Chimica Acta 2018; 483: 227-233.

[7] Zhang J and Li W. Long noncoding RNA CYTOR sponges miR-195 to modulate proliferation, migration, invasion and radiosensitivity in non-small cell lung cancer cells. Biosci Rep 2018; 38: BSR20181599.

[8] Hao W, Luo W, Bai M, Li J, Bai X, Guo J, Wu J and Wang M. MicroRNA-206 inhibited the progression of glioblastoma through BCL-2. J Mol Neurosci 2016; 60: 531-538.
[9] Chen Y, Xie H, Gao Q, Zhan H, Xiao H, Zou Y, Zhang F, Liu Y and Li J. Colon cancer associated transcripts in human cancers. Biomed Pharmacother 2017; 94: 531-540.
[10] Mengxiang Z, Nisha Z, Fengyao H, Song Y, Wang Z, Ni Y and Ding L. The regulatory role of non-coding RNAs on programmed cell death four in inflammation and cancer. Front Oncol 2019; 9: 919.
[11] Tang X, Qiao X, Chen C, Liu Y, Zhu J and Liu J. Regulation mechanism of long noncoding RNAs in colon cancer development and progression. Yonsei Med J 2019; 60: 319-325.
[12] Kondo Y, Shinjo K and Katsushima K. Long non-coding RNAs as an epigenetic regulator in human cancers. Cancer Sci 2017; 108: 1927-1933.
[13] Huang JZ, Chen M, Chen D, Gao X, Zhu S, Huang H, Hu M, Zhu H and Yan G. A peptide encoded by a putative lncRNA HOXB-AS3 suppresses colon cancer growth. Mol Cell 2017; 68: 171-184.
[14] Xue W, Yu H, Sun W, Kong J, Zhang L, Tang J, Wang J, Xu E, Lai M and Zhang H. The long non-coding RNA CYTOR drives colorectal cancer progression by interacting with NCL and Sam68. Mol Cancer 2018; 17: 110.
[15] Yue B, Liu C, Sun H, Liu M, Song C, Cui R, Qiu S and Zhong M. A positive feed-forward loop between LncRNA-CYTOR and Wnt/β-catenin signaling promotes metastasis of colon cancer. Mol Ther 2018; 26: 1287-1298.
[16] Zhu Z, Dai J, Liao Y, Ma J and Zhou W. Knockdown of long noncoding RNA LINC00152 suppresses cellular proliferation and invasion in glioma cells by regulating miR-4775. Oncol Res 2018; 26: 857-867.
[17] Wang H, Chen W, Yang P, Zhou J, Wang K and Tao Q. Knockdown of linc00152 inhibits the progression of gastric cancer by regulating microRNA-193b-3p/ETS1 axis. Cancer Biol Ther 2019; 20: 461-473.
[18] Zhang Y, Xiang C, Wang Y, Duan Y, Liu C, Jin Y and Zhang Y. LncRNA LINC00152 knockdown had effects to suppress biological activity of lung cancer through EGFR/PI3K/AKT pathway. Biomed Pharmacother 2017; 94: 644-651.
[19] Christos A, Kai W and Jose B. Urinary MicroRNA profiling predicts the development of microalbuminuria in patients with type 1 diabetes. J Clin Med 2015; 4: 1498-517.
[20] Ruixiang G, Zhen W, Qiang L and Yang C. MicroRNA-105 plays an independent prognostic role in esophageal cancer and acts as an oncogene. Cancer Biomark 2020; 27: 173-180.
[21] Zhiqiang W, Jiru ZM and Bo Y. Long intergenic noncoding RNA 00261 acts as a tumor suppressor in non-small cell lung cancer through regulating miR-105/FHL1 axis. J Cancer 2019; 10: 6414-6421.