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LncRNA NR027113 promotes malignant progression of gastric carcinoma *via* EMT signaling pathway

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Abstract. – OBJECTIVE: The aim of this study was to explore the characteristics of long non-coding RNA (lncRNA) NR027113 in gastric carcinoma, and to further investigate whether it could promote the development of gastric carcinoma *via* epithelial mesenchymal transition (EMT) signaling pathway.

PATIENTS AND METHODS: Quantitative Real-time polymerase chain reaction (qRT-PCR) was performed to analyze the expression of NR027113 in 68 paired of gastric carcinoma and para-carcinoma tissues. Subsequently, the relationship between NR027113 expression and clinical indexes of gastric carcinoma as well as the prognosis of patients was analyzed. NR027113 expression in gastric carcinoma cells was detected by qRT-PCR as well. NR027113 knockdown model was constructed by lentivirus transfection in gastric carcinoma cells (including AGS and SGC-7901). Meanwhile, the effects of NR027113 on the biological functions of gastric carcinoma cells were analyzed by cell counting kit-8 (CCK-8), wound healing, transwell invasion and migration assay, respectively. Furthermore, the correlation between NR027113 and EMT signaling pathways was studied.

RESULTS: QRT-PCR results showed that the expression level of NR027113 in gastric carcinoma tissues was significantly higher than that of para-carcinoma tissues. Compared with patients with low expression of NR027113, the incidence of lymph node metastasis and distant metastasis was significantly higher in patients with high NR027113 expression. Meanwhile, the survival rate of patients with low NR027113 expression was significantly lower. Compared with control group, the invasion and migration abilities of cells in NR027113 knockdown group were significantly decreased. Subsequent qRT-PCR results demonstrated that the expression of EMT signaling pathway-related proteins was significantly changed after transfection of sh-NR027113. The above finding indicated that NR027113 could inhibit the malignant progression of gastric carcinoma. Moreover, the addition of transforming growth factor-β (TGF-β) cytokines synergistically promoted the malignant progression of gastric carcinoma with NR027113.

CONCLUSIONS: NR027113 expression was significantly increased in gastric carcinoma. Meanwhile, it was positively correlated with lymph node metastasis, distant metastasis and poor prognosis of gastric carcinoma patients. Furthermore, NR027113 could accelerate the invasion and migration abilities of gastric carcinoma cells via EMT signaling pathway.

Key Words:
NR027113, MiRNA-140, Gastric carcinoma, Invasion, Migration.

Introduction

Gastric carcinoma is a high-risk gastrointestinal malignant tumor around the world. Its incidence rate and mortality rate rank the fourth and second among all cancers, respectively. Meanwhile, gastric carcinoma remains the major threat to human health, bringing huge economic and medical burden[1,2]. In China, about 400,000 new cases occur every year, accounting for about half of the total number of patients worldwide. Statistics have reported that its mortality rate ranks the second in females, only after gastric carcinoma and also ranks the second in males, only after lung cancer[3,4]. Previous studies have indicated that the pathogenic factors of gastric carcinoma are various, and the development process is complicated. Smoking, long-term consumption of fried and high-salt and high-fat food, and chronic infection of *Helicobacter pylori* are considered as significant risks for gastric carcinoma[3,4]. Most patients are not diagnosed until the middle and late stages due to various reasons. For example,

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early symptoms of gastric carcinoma are insidious, and the invasion and metastasis may develop quickly. The invasiveness of gastroscopy limits its application to a certain extent. Meanwhile, the sensitivity and specificity of existing serological tumor indicators are not high. All the above characteristics lead to poor prognosis and relatively short survival period of patients with gastric carcinoma[5-8]. Therefore, studying the mechanism of the incidence and development of gastric carcinoma and looking for novel tumor markers are of great significance for early diagnosis, treatment and prognosis monitoring of patients. This may also be helpful for finding new therapeutic targets for gastric carcinoma[9,10]. The Human Genome Project has shown that genes that encode proteins account for only 2% of the entire genome. The remaining 98% of the genes are known as non-coding RNAs. Depending on the length of nucleotide sequence, non-coding RNA can be divided into short non-coding RNA and long non-coding RNA (lncRNA)[11, 12]. LncRNA refers to a subclass of RNAs with no less than 200 nucleotides in length, which lack open reading frames and do not encode proteins[13-15]. Recently, more and more studies have confirmed that lncRNA participates in the normal growth and development and physiological processes of organisms *via* various biological processes, such as selective splicing, RNA transcription and degradation, and epigenetic modification. Meanwhile, lncRNA also plays an important role in the occurrence and development of multiple diseases[15,16]. Previous studies have suggested that NR027113 promotes the development of some human tumors. However, the specific mechanism remains elusive. Furthermore, the exact role of NR027113 in gastric carcinoma is still unknown[17]. High invasiveness and metastasis are one of the main features of gastric carcinoma. The above process involves changes in multiple gene expression and regulation of multiple signal transduction pathways[18,19]. Epithelial mesenchymal transition (EMT) is reported as one of the key mechanisms of invasion and metastasis[20,21]. The triggering of EMT is usually accompanied by changes in cell morphology and molecular markers in tumor cells, such as decreased expression of E-cadherin, claudin, and occludin. Eventually, this may lead to destruction of cell polarity[20]. Meanwhile, EMT can also cause the degradation of extracellular matrix and basement membrane. This can effectively damage and destroy the histological barrier that blocks the invasion of tumor cells, resulting tumor cells detach from the primary site to surrounding or distant tissues[22,23]. Therefore, in this study, we investigated whether lncRNA NR027113 could regulate the molecular mechanism of EMT-mediated invasion and metastasis of gastric carcinoma. Our findings might provide an experimental basis for the clinical application of NR027113.

Patients and Methods

Patients and Tissue Samples

In this study, 68 pairs of gastric carcinoma and para-carcinoma tissue samples were collected from patients who received surgical treatment. Collected tissues were restored at -80°C for subsequent use. This study was approved by the Ethics Monitoring Committee. Signed informed consent was obtained from each subject before the study.

Cell Culture

Human gastric carcinoma cell lines (including AGS, BGC-823, SGC-7901) and normal immortalized gastric mucosal epithelial cell line (GES-1) were obtained from American Type Culture Collection (ATCC) (Manassas, VA, USA). All cells were cultured in Dulbecco's whole modified MEM medium (DMEM) (Gibco, Rockville, MD, USA) containing streptomycin (100 μg/mL), penicillin (100 U/mL) and 10% fetal calf serum (FCS) (Gibco, Rockville, MD, USA) in a 37°C, 5% CO_2 incubator. When grown to 80-90% confluence, the cells were passaged to 1% trypsin + EDTA (Ethylene Diamine Tetraacetic Acid) for digestion.

Immunohistochemical Staining

After dewaxing and hydration, 50 μL of anti-rat ki-67 (1:100) was added dropwise. The mixture was incubated for 1 h at room temperature. After washing with phosphate-buffered saline (PBS) for 3 times (5 min for each time), corresponding secondary antibody was added dropwise, followed by 1 h of incubation at room temperature. Next, the samples were stained with diaminobenzidine (DAB) (Solarbio, Beijing, China) for 5-10 min, and the degree of staining was controlled under a microscope. After rinsing with deionized water for 10 min, the samples were counterstained with hematoxylin for 2 min and differentiated by hydrochloric acid alcohol. Then the samples were rinsed with deionized water for 10-15 min again. Finally, the samples were observed under a microscope after dehydration, transparent, and sealing.

Cell Transfection

Lentivirus containing NR027113 knockdown sequence (sh-NR027113) and corresponding negative control (shRNA) were purchased from Shanghai Jima Company (Shanghai, China). Cells were first seeded into 6-well plates and grown to the density of 40%. Then cell transfection was performed according to the manufacturer's instructions. After 48 h, transfected cells were collected for quantitative Real-time polymerase chain reaction (qRT-PCR) analysis and cell function experiments.

Cell Proliferation Assay

48 h after transfection, the cells were collected and seeded into 96-well plates at a density of 2000 cells per well. After culture for 24 h, 48 h, 72 h and 96 h, respectively, cell counting kit-8 (CCK-8) (Dojindo Laboratories, Kumamoto, Japan) reagent was added in each well. After incubation for 2 hours, optical density (OD) value of each well at the wavelength of 490 nm was detected by a microplate reader.

Transwell Cell Migration and Invasion Assay

48 hours after transfection, the cells were digested, centrifuged and re-suspended in FBS-free culture. Cell density was adjusted to $5^{*}10^{5}$ cells/mL. 200 μL of cell suspension ($1^{*}10^{5}$ cells) was added to the upper chamber, meanwhile, 700 μL of medium containing 20% fetal bovine serum (FBS) was added to the lower chamber. According to different migration abilities, the cells were placed in an incubator, followed by culture for a specific time. After that, transwell chambers were taken out, washed 3 times with 1* PBS, and fixed with methanol. After staining with 0.2% crystal violet for 20 min, the cells on the chamber surface were removed with water and a cotton swab carefully. Perforated cells stained in the outer layer of the basement membrane of the chamber were observed under a microscope. 5 fields of view were randomly selected for each sample.

Wound Healing Assay

48 hours after transfection, the cells were digested, centrifuged and re-suspended in FBS-free culture to adjust $5^{*}10^{5}$ cells/mL of cell density. The density of plated cells was determined according to the size of cells (the majority of the number of cells plated was set to 50,000 cells/well). On the next day, the confluence of cells reached 90% or more. After scribing, the cells were rinsed gently with PBS for 2-3 times. Subsequently, low concentration of serum medium (such as 1% FBS) was added, and the cells were observed again after 24 hours. According to the pre-experiment of this assay, cell-healing ability was judged according to the migration areas. For the formal experiment, the difference of cell healing ability was judged according to the migration areas.

QRT-PCR

1 mL of TRIzol Reagent (Invitrogen, Carlsbad, CA, USA) was added to lyse cells, and total RNA was extracted. Initially extracted RNA was treated with DNase I to wipe off genomic DNA and re-purify the RNA. RNA reverse transcription was performed according to the instructions of Prime Scirpt Reverse Transcription Kit (TaKaRa, Otsu, Shiga, Japan). Real-time PCR was performed according to the SYBR® Premix Ex TaqTM (TaKaRa, Otsu, Shiga, Japan) kit instructions. The reaction was performed by StepOne Plus Real-time PCR System (Applied Biosystems, Foster City, CA, USA). Primers used in this study were as follows: NR027113: forward: 5'-ACCAATCACATAGCCCTGCC-3', reverse: 5'-TCAGAGCTGCAGATGTGGTC-3'; Glyceraldehyde 3-phosphate dehydrogenase (GAPDH): forward: 5'-CGCTCTCTGCTCCTCCTGTTC-3', reverse: 5'-ATCCGTTGACTCCGACCTTCAC-3'. Each sample was subjected to a three-well repeated experiment and repeated twice. Bio-Rad PCR instrument was used to analyze and process data with iQ5 2.0 software (Hercules, CA, USA). GAPDH and U6 genes were used as internal references. Expression level of genes was calculated by the $2^{-\Delta\Delta Ct}$ method.

Western Blot

Transfected cells were first lysed with cell lysis buffer, shaken on the ice for 30 minutes, and centrifuged at 14,000*g at 4°C for 15 minutes. The concentration of extracted total protein was calculated by the HCCA Protein Assay Kit (Pierce, Rockford, IL, USA). After separation by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) electrophoresis, the membranes were transferred onto membranes. After blocking overnight, the membranes were incubated with primary and secondary antibodies. Finally, immuno-reactive bands were visualized by the enhanced chemiluminescence (ECL) coloration. The image was semi-quantitatively analyzed by alpha SP image analysis software (Broomfield, CO, USA). E-cadherin, N-cadher-

in, Vimentin, TGF-β, MMP-9 rabbit anti-human monoclonal antibodies were obtained from Santa Cruz, Biotechnology (Santa Cruz, CA, USA). Horseradish peroxidase (HRP) -labeled goat anti-rabbit secondary antibody was obtained from Genscript (Nanjing, China). GAPDH was used an internal control. This experiment was repeated for three times.

Statistical Analysis

GraphPad Prism 5 V5.01 software (La Jolla, CA, USA) was used for all statistical analysis. Student's *t*-test was performed to compare the difference between two groups. One-way analysis of variance (ANOVA) was used to compare the difference among different groups, followed by Post-Hoc Test (Least Significant Difference). Experimental data were expressed as mean ± standard deviation ($\bar{x}\pm s$). There were three levels of significant difference, including $p<0.05$, $p<0.01$ and $p<0.001$ $p<0.05$ was considered statistically different.

Results

NR027113 Was Highly Expressed in Gastric Carcinoma Tissues and Cells

To explain the role of NR027113 in gastric carcinoma, we first collected 68 pairs of gastric carcinoma and para-carcinoma tissues. NR027113 expression in above tissues was then detected by qRT-PCR. The results showed that NR027113 was significantly up-regulated in gastric carcinoma tissues when compared with para-carcinoma tissues (Figure 1A). In addition, compared with GES-1 cells, NR027113 was highly expressed in gastric carcinoma cells. The above findings suggested that NR027113 played an oncogene role in gastric carcinoma (Figure 1B). At the same time, we detected ki-67 expression in gastric carcinoma and para-carcinoma tissues using immunohistochemistry. Results found that expression of Ki-67 in gastric carcinoma tissues was significantly increased (Figure 1C).

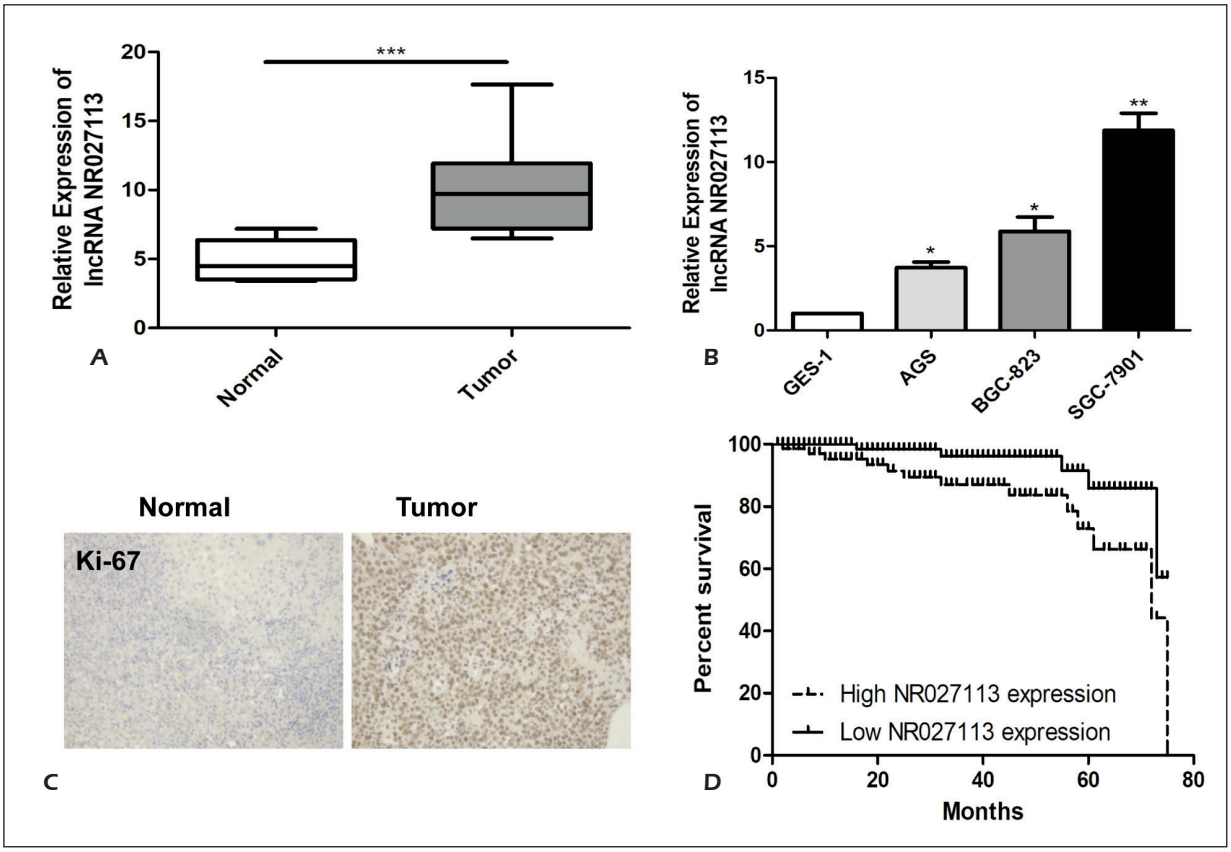

Figure 1. NR027113 was highly expressed in gastric carcinoma tissues and cells. **A**, QRT-PCR was applied to detect NR027113 expression in gastric carcinoma and para-carcinoma tissues; **B**, QRT-PCR was used to detect the expression level of NR027113 in gastric carcinoma cells; **C**, Immunohistochemistry analysis of ki-67 in gastric carcinoma and adjacent non-cancerous tissues; **D**, Kaplan Meier survival curve of gastric carcinoma patients based on NR027113 expression. The prognosis of patients with higher expression was significantly worse than those with lower expression. Data were represented as mean ± SD, *$p<0.05$, **$p<0.01$, ***$p<0.001$.

NR027113 Expression was Correlated With Distance Metastasis, Lymph Node and Overall Survival of Gastric Carcinoma Patients

Based on the mRNA expression of NR027113 in 68 gastric carcinoma and para-carcinoma tissues, these patients were divided into high expression and low expression groups. Subsequently, the association between NR027113 expression and age, sex, pathological stage, lymph node metastasis and distant metastasis of patients with gastric carcinoma was explored. As shown in Table I, high expression of NR027113 was positively correlated with lymph node metastasis and distant metastasis of gastric carcinoma, whereas was not correlated with age, gender, and pathological stage. To further figure out the relationship between the expression of NR027113 and the prognosis of patients with gastric carcinoma, relevant follow-up data was collected. Kaplan-Meier survival curves indicated that high expression of NR027113 was highly associated with poor prognosis of gastric carcinoma. Higher expression level of NR027113 indicated significantly worse prognosis of patients ($p<0.05$; Figure 1D).

Knockdown of NR027113 Inhibited Cell Proliferation

To explain the function of NR027113 in gastric carcinoma, we first constructed a lentiviral vector containing sh-NR027113 sequence. After transfection of NR027113 lentiviral vector in AGS and SGC-7901 cells, qRT-PCR was performed to verify the interference efficiency (Figure 2A). The results of CCK-8 assay suggested that the proliferation rate of cells in sh-NR027113 group was dramatically lower than that of control group, and the difference was statistically significant (Figure 2B). Meanwhile, NR027113 was knocked down in AGS and SGC-7901 cells, transwell migration, invasion and cell scratch experiments were performed to detect cell invasion and migration abilities. The results showed that compared with control group, the invasion and migration of cells in sh-NR027113 group was significantly decreased (Figure 2C). In addition, wound-healing assay also reflected a significant decrease in the crawling ability of gastric carcinoma cells after NR027113 inhibition (Figure 2D).

Down-Regulation of NR027113 Decreased the Expression of EMT Signaling Pathway

To further explore the mechanism of NR027113 in promoting the malignant progression of gastric carcinoma, we examined the expressions of key proteins in EMT-related pathways after silence of NR027113 through Western Blot. The results showed that silence of NR027113 significantly increased the protein expression of E-cadherin. It is known that E-cadherin is one of the most important markers in EMT signaling pathway. However, the expressions of other proteins such as N-cadherin, Vimentin, TGF-β, and MMP-9 were significantly decreased. Therefore, the development of gastric carcinoma was promoted (Figure 3).

Table I. Association of lncRNA NR027113 expression with clinicopathologic characteristics of gastric cancer.

Parameters	Number of cases	SNHG20 expression		*p*-value
		Low (%)	High (%)	
Age (years)			0.220	
< 60	29	17	12	
≥ 60	39	17	22	
Gender			0.332	
Male	34	19	15	
Female	34	15	19	
T stage			0.220	
T1-T2	39	22	17	
T3-T4	29	12	17	
Lymph node metastasis			0.013	
No	42	26	16	
Yes	26	818		
Distance metastasis			0.007	
No	39	25	14	
Yes	29	920		

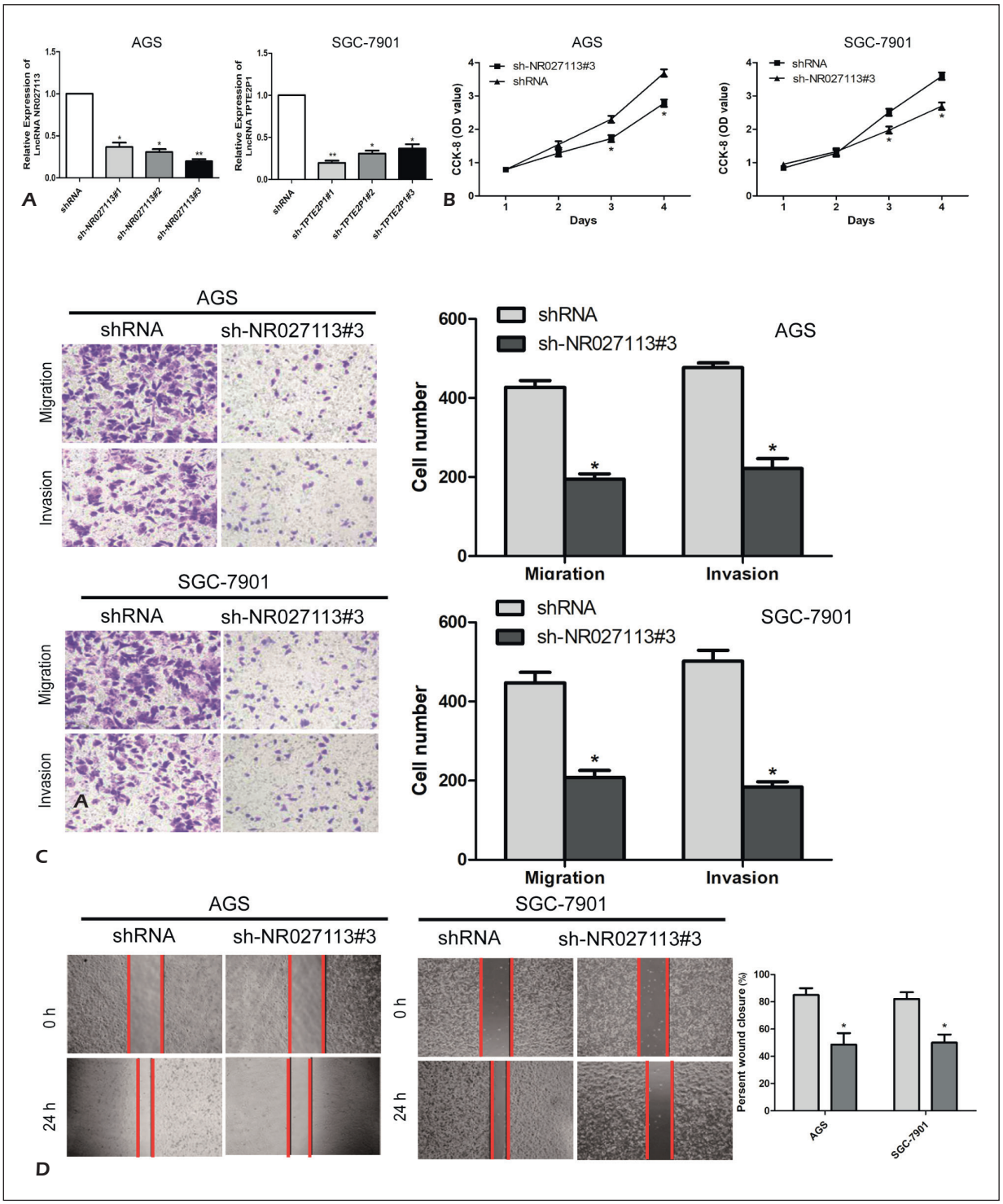

Figure 2. Silence of NR027113 inhibited the migration and invasion of gastric carcinoma cells. **A**, QRT-PCR was applied to verify the interference efficiency after transfection of NR027113 knockout vector in AGS and SGC-7901 cells; **B**, CCK-8 assay was performed in AGS and SGC-7901 cells to detect the influence of NR027113 on cell proliferation; **C**, Transwell migration and invasion experiments were applied to detect the migration and invasion abilities of AGS and SGC-7901 cells; **D**, Wound healing test in AGS and SGC-7901 cells. Data were represented as mean ± SD, *p<0.05.

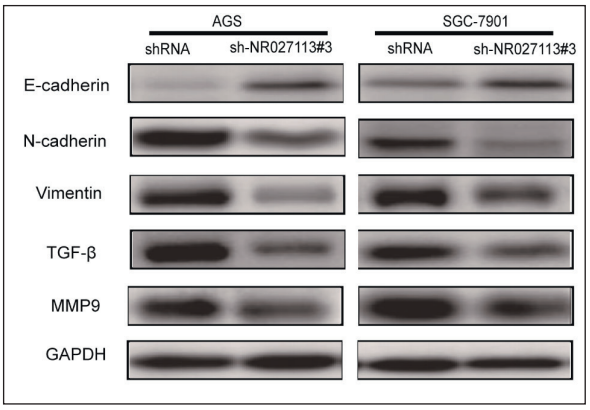

Figure 3. Mechanism of silencing NR027113 by regulating EMT signaling pathway. Western blot was applied to verify the expressions of E-cadherin, N-cadherin, Vimentin, TGF-β, and MMP-9 after interference with NR027113 in AGS and SGC-7901 cells.

NR027113 Modulated TGF-β Expression in Human Gastric Carcinoma Cells

To further explore the way in which NR027113 facilitated the malignant progression of gastric carcinoma, we explored the possible relationship between NR027113 and EMT signaling pathways *via* Western blot. TGF-β is one of the signal molecules in EMT signaling pathway. Subsequently, TGF-β cytokine was added to NR027113 silenced gastric carcinoma cells to explore the interaction between NR027113 and TGF-β. QRT-PCR and Western blot were applied to compare the changes in the expression of NR027113 and TGF-β in cells of sh-NR027113 group and sh-NR027113+TGF-β group (Figure 4A, 4B). Transwell migration, invasion and wound healing experiments demonstrated that TGF-β synergistically promoted the effect of NR027113 on the invasion and migration of gastric carcinoma cells (Figure 4C and 4D). In addition, our findings revealed that compared with sh-NR027113 group, E-cadherin expression in cells of sh-NR027113+TGF-β group was remarkably decreased, whereas the expressions of other proteins (including N-cadherin, Vimentin, TGF-β and MMP-9) were significantly increased (Figure 4E).

Discussion

As a highly occurring cancer worldwide, gastric carcinoma ranks the second and third among Chinese male and female cancer patients over the past 10 years. Meanwhile, its mortality rate ranks the second among Chinese cancer populations[2-4]. Although early diagnosis and treatment can greatly improve patients' postoperative survival, gastroscopy examination is not suitable for mass screening due to its invasiveness. Therefore, it is of great significance to search for serological tumor markers for early diagnosis, and to improve post-operative and post-chemotherapy efficacy[5,6]. So far, no specific gastric carcinoma tumor markers have been found. Moreover, the sensitivity and specificity of widely used gastric carcinoma diagnostic indicators, such as CEA and CA72.4, need to be improved[7-9]. LncRNA is a kind of RNA with about over than 200 nucleotides in length. These RNAs do not have the function of encoding proteins. Existing studies have shown that lncRNA is correlated with the occurrence and development of malignant tumors. The role of some lncRNA molecules, such as H19 and HOX transcriptional antisense RNA (HOTAIR), has been verified in malignancies. In this study, we aimed to find out tumor serological markers in lncRNA molecules for early diagnosis and therapy of gastric carcinoma[9-12]. A plenty of studies have shown that lncRNA plays an important role in the occurrence and development of gastric carcinoma. Numerous lncRNAs are found abnormally expressed in tissue samples and plasma samples of patients[10-12]. A small number of gastric carcinoma-related lncRNAs have carcinogenic or tumor suppressor activity. Meanwhile, they take an essential part in the pathogenesis of gastric carcinoma, which may become a potential diagnostic marker and therapeutic target[13-15]. NR027113 is a newly discovered long-chain non-coding RNA. Studies have indicated that NR027113 is highly expressed in liver cancer. Meanwhile, its high expression is correlated with poor prognosis of patients with liver cancer. However, few reports have investigated the role of NR027113 in the malignant progression of gastric cancer[17]. In the current study, bioinformatics analysis was used to analyze the difference of lncRNA expression between AGS and SGC-7901cells. NR027113 was selected as a candidate that might be associated with the malignant progression of gastric carcinoma. Subsequently, the relationship between NR027113 expression and the development of gastric carcinoma was determined. Up-regulation of NR027113 was confirmed to promote the malignant progression of gastric carcinoma. Meanwhile, we found that NR027113 expression in gastric carcinoma tissues was remarkably higher than of para-carcinoma tissues. High expression of NR027113 was also correlated with tumor stages and poor prognosis of patients with gastric carcinoma. The above findings suggested that NR027113 played an essential

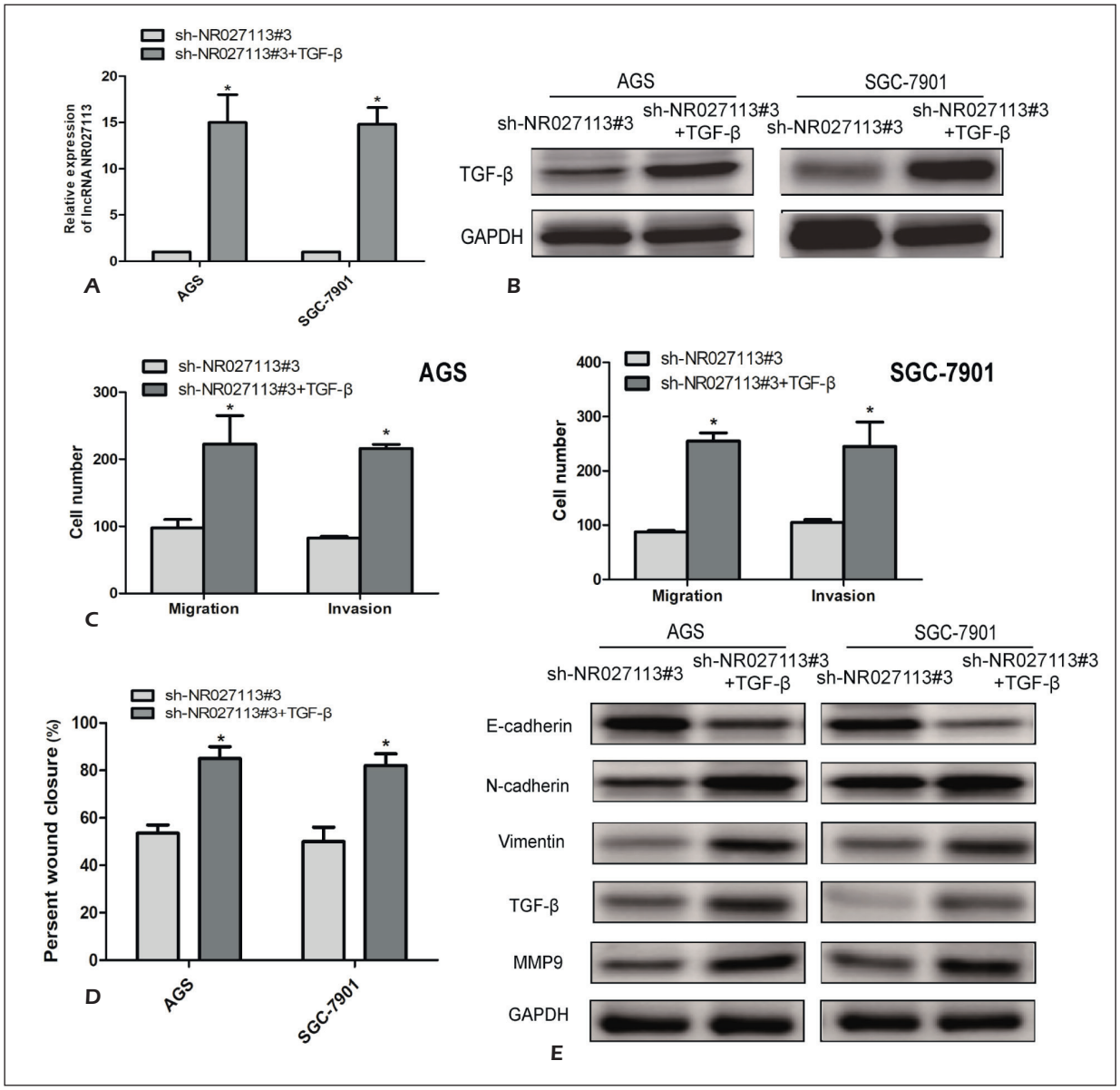

Figure 4. NR027113 regulated the expression of key protein of TGF-β in EMT signaling pathway. **A**, NR027113 expression in NR027113 and TGF-β cytokine stimulation was detected by qRT-PCR; **B**, TGF-β expression in NR027113 and TGF-β cytokine stimulation was detected by Western blotting; **C**, Transwell migration experiment was applied to detect the ability of NR027113 and TGF-β cytokines in stimulating migration and invasion of AGS and SGC-7901 cells; **D**, Wound healing test was performed to detect the effects of NR027113 and TGF-β cytokine co-stimulation on crawling ability in AGS and SGC-7901 cells; **E**, Western blot was performed to verify the expressions of E-cadherin, N-cadherin, Vimentin, TGF-β and MMP-9 after co-stimulation of NR027113 and TGF-β cytokines in AGS and SGC-7901 cells. Data were represented as mean ± SD, *$p<0.05$.

role in promoting the development of gastric carcinoma. To explore the effect of NR027113 on the migration and invasion of gastric carcinoma cells, transwell migration invasion and wound healing assay were performed in AGS and SGC-7901 cells. Results found that compared with cells in shRNA group, the migration and colony formation abilities of cells in NR027113 inhibiting group were weakened obviously. This confirmed that sh-NR027113 could inhibit the invasion and migration abilities of AGS and SGC-7901 cells. Conversely, these findings demonstrated that NR027113 could accelerate cell invasion and migration abilities. This study provided a theoretical basis for revealing the occurrence and development mechanism of gastric cancer. However, the specific molecular

mechanism of signal transduction needed further study. EMT can reduce the expression of multiple linker molecules in epithelial cells (such as E-cadherin, claudin and occludin), thus destroying cell polarity[18-20]. In addition, EMT induces partial degradation of extracellular matrix and basement membrane, forming an effective destruction of the extracellular histological barrier. This is more conducive to the invasive ability of tumor cells, allowing them to escape. Subsequently, *in situ* tumor or other distal normal tissues are more prone to invasion and metastasis[21]. EMT is characterized by reduced cell adhesion and morphological changes, as well as enhanced expressions of epithelial and mesenchymal-related genes[22]. In the current study, we proved that EMT was abnormally activated in the progression and development of gastric cancer. This resulted in a rise in the number of cells with mesenchymal characteristics and a reduction in the number of epithelial cells. Ultimately, this may promote the metastasis and invasion of gastric carcinoma[23]. However, so far, the relevant mechanisms in the progression and development of gastric carcinoma have not yet been fully elucidated. To further explore the regulatory relationship of NR027113 and EMT signaling pathway in gastric carcinoma cells, we knocked down NR027113. Results found that silence of NR027113 significantly elevated the expression of E-cadherin in the EMT signaling pathway. However, the expressions of other proteins, such as N-cadherin, Vimentin, TGF-β and MMP-9, were significantly reduced. The development of gastric carcinoma was thereby promoted. In addition, studies have revealed that the addition of cytokine TGF-β synergistically promotes the role of NR027113 in gastric carcinoma cells. This evidence suggests that the transcriptional activity of NR027113 locus may be regulated by the key protein of TGF-β in the EMT signaling pathway. The above findings all demonstrated that NR027113 accelerated the migration and invasion of gastric carcinoma cells through targeting genes in the EMT signaling pathway.

Conclusions

LncRNA NR027113 was significantly up-regulated in both gastric carcinoma tissues and cells. Meanwhile, its expression was correlated with lymph node metastasis, distant metastasis and poor prognosis of patients. In addition, NR027113 might accelerate the invasion and migration of gastric carcinoma *via* EMT signaling pathway.

Conflict of Interests

The authors declared no conflict of interest.

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