Int J Clin Exp Med 2019;12(5):5341-5348
www.ijcem.com /ISSN:1940-5901/IJCEM0087235

Original Article

miR-106 serves as a prognostic biomarker for gastric cancer and promotes cancer progression

Xuemei Zhang[1], Wenqi Song[2], Yanli Zhu[1], Zhuoxin Cheng[3], Shihua Zhang[4], Qianzi Liu[5]

[1]Department of Gastroenterology, First Affiliated Hospital of Jiamusi University, Jiamusi 154002, Heilongjiang, China; [2]Department of Pharmacy, Jiamusi Central Hospital, Jiamusi 154002, Heilongjiang, China; [3]Department of General Surgery, First Affiliated Hospital of Jiamusi University, Jiamusi 154002, Heilongjiang, China; [4]Department of Brain surgery, First Affiliated Hospital of Jiamusi University, Jiamusi 154002, Heilongjiang, China; [5]Department of Pharmacy, School Clinic of Jiamusi University, Jiamusi 154002, Heilongjiang, China

Received October 24, 2018; Accepted December 9, 2018; Epub May 15, 2019; Published May 30, 2019

Abstract: MicroRNAs (miRNAs) have been shown play crucial roles in tumorigenesis and tumor progression. The aim of this study was to investigate the expression pattern, clinical value, and functional roles of miR-106 in gastric cancer. Expression of miR-106 was detected by quantitative real-time PCR. Kaplan-Meier and Cox regression analyses were performed to estimate the potential prognostic value of miR-106 in gastric cancer. Cell experiments were carried out to explore the functional roles of miR-106. Expression of miR-106 was significantly increased in gastric cancer tissues and cell lines, compared with controls (all $P < 0.05$). Increased miR-106 expression was significantly associated with lymph node metastasis and TNM stage. High miR-106 expression predicted shorter overall survival, compared with low expression levels (log-rank $P = 0.028$). Multivariate Cox regression analysis results showed that miR-106 was an independent prognostic factor for patients. Cell experiments demonstrated that cell proliferation, migration, and invasion were enhanced by upregulation of miR-106 expression, but were suppressed by reduction of miR-106 expression (all $P < 0.05$). Overexpression of miR-106 may serve as an independent prognostic biomarker of gastric cancer and promote tumor progression.

Keywords: microRNA-160, gastric cancer, prognosis, progression

Introduction

Gastric cancer is a leading cause of cancer-related mortality in the digestive system, worldwide. Its high mortality rate can be observed in Eastern Asian, Eastern Europe, and South America, likely due to both environmental and social factors [1, 2]. Although incidence of gastric cancer is now in a declining trend and the survival rates are rising, the mortality of gastric cancer patients remain high in China [3, 4]. Prognosis of gastric cancer at an advanced stage remain poor, with a 5-year survival rate below 40% [3]. Thus, identification of tumor biomarkers and therapeutic targets is essential for gastric cancer patients.

MicroRNAs (miRNAs) are a class of small non-coding RNAs that are approximately 22 nucleotides in length. They regulate target gene expression post-transcriptionally through targeting the 3'-untranslated region (3'-UTR) of target mRNAs [5]. An increasing number of studies have demonstrated that miRNAs function as a tumor suppressor or oncogenes in tumorigenesis, serving as key regulators in various biological processes, including cell proliferation, migration, invasion, and apoptosis [6, 7]. More importantly, some specific miRNAs and their targets have been reported to play important roles in the development and progression of various types of human cancer, including gastric cancer [8-10]. For instance, serum miR-106 was found to be upregulated in gastric cancer. It could be a novel non-invasive biomarker for detection of gastric cancer [11]. Another study showed that serum miR-106 was upregulated in gastric cancer [12]. However, expression patterns of miR-106 in gastric cancer tissues and its biological roles in gastric cancer require further investigation.

The current study investigated expression levels of miR-106 in gastric cancer tissues and adjacent non-tumor tissue samples and cell lines. The prognostic significance of miR-106 in

Table 1. Correlation of miR-106 expression with clinical features of gastric cancer patients

Parameters	Cases No. (n = 132)	miR-106 expression		*P*
		Low (n = 61)	High (n = 71)	
Gender				0.186
Male	92	46	46	
Female	40	15	25	
Age				0.232
< 60	68	28	40	
≥ 60	64	33	31	
Tumor size				0.510
< 3 cm	63	31	32	
≥ 3 cm	69	30	39	
Differentiation				0.563
Moderate + Well	70	34	36	
Poor	62	27	35	
Local invasion				0.097
T1-T2	72	38	34	
T3-T4	60	23	37	
Lymph node metastasis				0.025
Negative	64	36	28	
Positive	68	25	43	
TNM stage				0.015
I-II	65	37	28	
III-IV	67	24	43	

gastric cancer was also assessed. The aim of this study was to examine the roles of miR-106 in human gastric cancer.

Materials and methods

Patients and specimens

A total of 132 paired human gastric cancer tissues and adjacent non-tumor tissue specimens were collected from gastric cancer patients that underwent surgery at First Affiliated Hospital of Jiamusi University, between 2008 and 2012. All tissue specimens were verified by experienced pathologists. No patients received any preoperative therapy. Gastric cancer tissues and normal tissue specimens were snap frozen immediately in liquid nitrogen and stored at -80°C until total RNA was extracted. Clinicopathological characteristics of the gastric cancer patients were collected and are listed in **Table 1**. Written informed consent was obtained from each patient participating in this study. The present study was approved by the Ethics Committee of First Affiliated Hospital of Jiamusi University. Five-year follow-up information was collected by telephone for subsequent analysis.

Cell lines and transfection

Human gastric cancer cell lines (MGC-803, AGC, SGC-7901, and BGC-823) and one normal gastric epithelium cell line (GES-1) were purchased from Cell Bank of Chinese Academy of Sciences (Shanghai, China). All cells were cultured in Gibco Dulbecco's modified Eagle's medium (DMEM, Thermo Fisher Scientific, Inc., Waltham, MA, USA), supplemented with heat-inactivated 10% fetal bovine serum (FBS) at 37°C in a humidified incubator with 5% CO_2. Cells were seeded at a density of 5×10^4 cells per well in 6-well plates and incubated for 24 hours. The cells were then transfected with the miR-106 mimic, mimic negative control (NC), miR-106 inhibitor, or inhibitor NC using Lipofectamine™ 2000 (Invitrogen; Thermo Fisher Scientific, Inc.), following manufacturer instructions. Untreated cells were used as blank control.

RNA extraction and reverse transcription-quantitative polymerase chain reaction (qRT-PCR)

Total RNA was extracted from the cell lines and tissue specimens using TRIzol Reagent (Invitrogen, Carlsbad, CA, USA), following manufacturer protocol. The purity of RNA was assessed by measuring absorbance at 260 nm and 280 nm. The ratio of OD was 260/280. Purified total RNA was then reverse transcribed to complementary DNA (cDNA) using the RevertAid First Strand cDNA Synthesis kit (Thermo Fisher Scientific, Inc.). Next, qRT-PCR was performed using SYBR Green Premix Ex Taq (Takara, Japan) on an Applied Biosystems 7500 Real-Time PCR System (Applied Biosystems, USA). Relative miR-106 expression was calculated with the $2^{-\Delta\Delta Ct}$ method and normalized to U6.

Cell proliferation assay

Cell proliferation was detected using the 3- (4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay. SGC-7901 and MGC-803 cells were seeded in 96-well plates with a density of 5,000 cells per well. After incubation

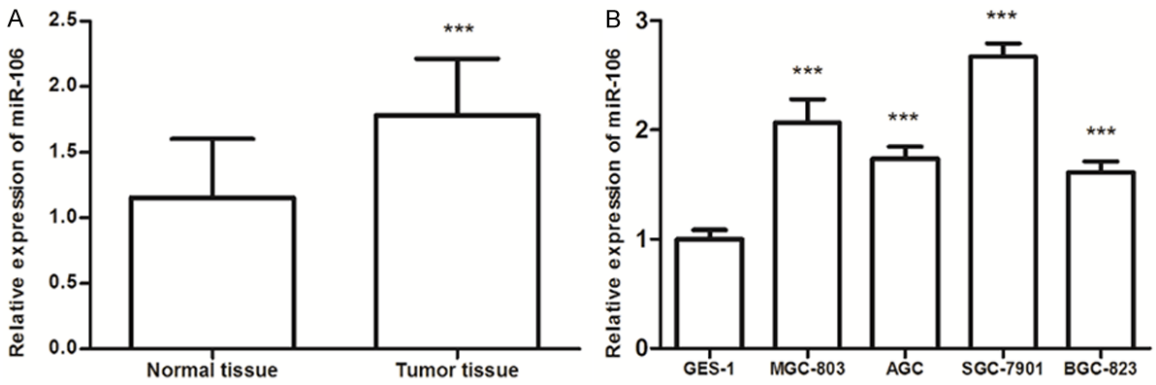

Figure 1. miR-106 was upregulated in gastric cancer tissues and cell lines. A. Relative expression of miR-106 in 132 pairs of gastric cancer tissues and their corresponding adjacent normal tissues. B. Expression of miR-106 in gastric cancer cell lines (MGC-803, AGC, SGC-7901, and BGC-823) and normal gastric epithelium cell line (GES-1). (***$P < 0.001$).

overnight, cells were transfected with miR-106 mimic, inhibitor, or their negative controls. The cells were cultured at 37°C for 1-4 days before the addition of 10 μL MTT (Sigma-Aldrich, 5 mg/mL) to the culture medium in each well. After 4 hours, the medium was removed and the precipitate was dissolved using 100 μL DMSO (Sigma-Aldrich). Absorbance was measured at a wavelength of 490 nm for each well.

Cell migration and invasion assays

Transwell assays were used with a 24-well Transwell chamber (8-μm pore size, Multiskan MK3, Thermo, Waltham, MA) to determine the migration and invasion capacities of transfected cells. For the migration assay, cells were added in the top chamber at a concentration of 1×10^4 per well. For the invasion assay, 5×10^4 cells were plated in the top compartment with the Matrigel-coated membrane (Bedford, MA, USA) on the upper side. Both assays were then incubated in serum-free DMEM medium at 37°C for 16 hours. The lower chamber was filled with 600 mL DMEM containing 10% FBS as a chemo-attractant. After incubation for 16 hours, the non-migrated/non-invaded cells were removed using a cotton swab. Cells that migrated/invaded into the lower compartment were fixed in 3.7% formaldehyde for 5 minutes and stained with 0.1% crystal violet for 15 minutes. The number of cells was counted under a microscope (Olympus, Tokyo, Japan).

Statistical analysis

SPSS 21.0 software (SPSS, Inc., Chicago, IL, USA) and GraphPad Prism 5.0 software (GraphPad Software, Inc., Chicago, USA) was used to perform all statistical analyses. Measurement data are presented as the mean ± standard deviation (SD). Data for groups were analyzed with paired Student's t-tests or one-way ANOVA. The relationship between clinicopathological characteristics of patients and miR-106 expression was analyzed by the χ^2 test. Kaplan-Meier and Cox regression analysis were used to analyze the clinical significance of miR-106 in gastric cancer. Statistical significance is indicated when P is less than 0.05. Each experiment in this study was repeated at least three times.

Results

Expression of miR-106 in tissue specimens and cells

To investigate the potential significance of miR-106 in the development of gastric cancer, expression levels of miR-106 in 132 paired gastric cancer tissues and adjacent normal tissue specimens were detected. Moreover, qRT-PCR results showed that miR-106 was indeed increased in tumor tissues, compared with that in adjacent normal tissue specimens ($P < 0.001$, **Figure 1A**). Expression of miR-106 was also detected in gastric cancer cell lines and normal cell lines. As shown in **Figure 1B**, expression of miR-106 was found markedly increased in all gastric cancer cell lines, compared with that in normal gastric epithelium cell line GES-1 (all $P < 0.001$).

Expression of miR-106 correlated with clinical characteristics of gastric cancer patients

This study further investigated the relationship between miR-106 and clinical features of gas-

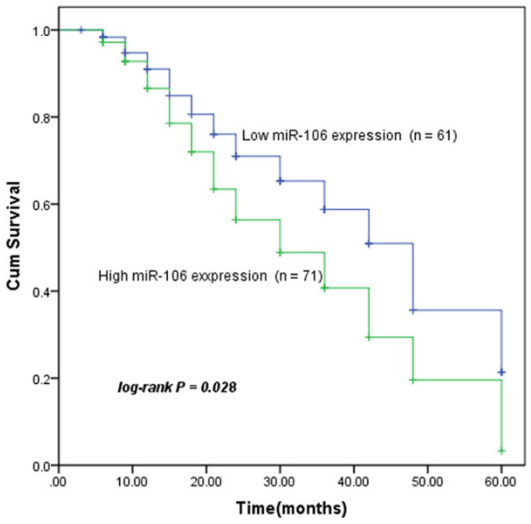

Figure 2. Analysis of the survival curve in 132 gastric cancer patients by Kaplan-Meier survival analysis. Patients with high miR-106 expression showed shorter overall survival than those with low expression levels.

tric cancer patients. All 132 patients were divided into two groups according to the mean value of relative expression levels of miR-106 (1.781) in cancer tissues, including the low miR-106 expression group and high miR-106 expression group. As shown in **Table 1**, high miR-106 expression in gastric cancer was notably correlated with lymph node metastasis (P = 0.025) and TNM stage (P = 0.015). However, miR-106 expression was not associated with other features, such as gender, age, tumor size, differentiation, and local invasion (all P > 0.05, **Table 1**).

Prognostic significance of miR-106 in gastric cancer

Kaplan-Meier analysis showed that survival times of patients with high miR-106 expression were shorter than in patients with low miR-106 expression (log-rank P = 0.028, **Figure 2**). Moreover, miR-106 expression and all clinical parameters were included in the Cox regression analysis to explore factors that had independent prognostic value on overall survival of gastric cancer patients. As shown in **Table 2**, miR-106 (HR = 1.190, 95% CI = 1.139-3.203, P = 0.014) was an independent prognostic factor for gastric cancer patients.

Table 2. Multivariate Cox analysis for miR-106 in gastric cancer patients

Characteristics	Multivariate analysis		
	HR	95% CI	P
miR-106	1.910	1.139-3.203	0.014
Gender	0.737	0.440-1.232	0.244
Age	1.382	0.858-2.226	0.183
Tumor size	0.827	0.517-1.323	0.428
Differentiation	0.682	0.411-1.132	0.139
Local invasion	0.871	0.533-1.423	0.580
Lymph node metastasis	0.977	0.590-1.620	0.929
TNM stage	0.989	0.610-1.603	0.964

Effects of miR-106 on cell proliferation, migration, and invasion

Increased expression of miR-106 in tumor specimens and the correlation with clinical characteristics of patients led to an investigation of the functional roles of miR-106 in gastric cancer, as well as its effects on tumor cell proliferation, migration, and invasion. These were examined using miR-106 mimics or miR-106 inhibitors. Gastric cancer cell lines MGC-803 and SGC-7901 were used in the cell experiments, as they had rather high miR-106 expression. Moreover, qRT-PCR results indicated that expression of miR-106 in gastric cancer cells transfected with the miR-106 mimics was significantly higher, while in cells transfected with miR-106 inhibitors it was reduced, compared to controls (all P < 0.05, **Figure 3A**). MTT assay was used to measure cell proliferation. Results showed that upregulation of miR-106 by miR-106 mimics promoted gastric cancer cell proliferation, while downregulation of miR-106 by miR-106 inhibitors inhibited cell proliferation, compared to controls (all P < 0.05, **Figure 3B**).

In addition to proliferation, cell migration and invasion were assessed using Transwell assays. Assay results indicated that gastric cancer cells transfected with miR-106 mimics promoted the capacities of migration and invasion, but cells transfected with miR-106 inhibitor decreased migration and invasion capacities, compared to controls (all P < 0.05, **Figure 4**).

Discussion

Surgical resection treatment remains the main therapy for gastric cancer. Even though a vari-

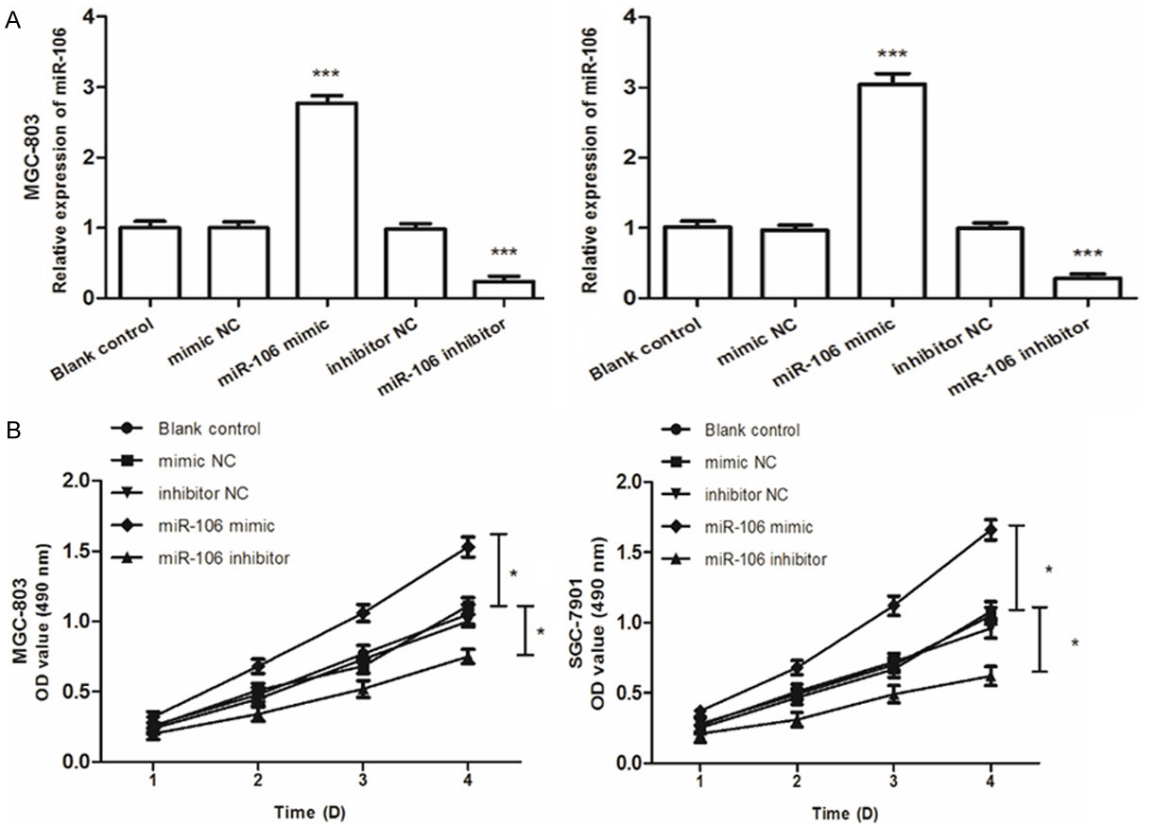

Figure 3. Effects of miR-106 on cell proliferation in MGC-803 and SGC-7901 cells. A. In the two cell lines, expression of miR-106 was markedly increased by miR-106 mimic but was decreased by the miR-106 inhibitor, compared with controls. (***$P < 0.001$). B. Proliferation ability was enhanced by overexpression of miR-106 but was suppressed by downregulation of miR-106. (*$P < 0.05$).

ety of comprehensive treatments, including surgery, chemotherapy, and radiotherapy, have been adopted, the 5-year survival rate of gastric cancer is still unsatisfactory. Many patients will have recurrence and metastasis after surgery [13, 14]. Numerous studies have indicated that biomarkers used for diagnosis and/or prognosis demonstrate high potential to improve outcomes of cancer patients [15-18]. In gastric cancer, some diagnostic or prognostic biomarkers have also been investigated. For instance, the NOB1 gene was found to be correlated with clinical outcomes and prognosis of gastric cancer patients, suggesting that it was an independent risk factor for 5-year mortality of patients. This provides more clinical evidence for it as a new target for diagnosis and treatment for gastric cancer [19]. A study by Yörüker EE et al. identified that circulating lncRNA H19 was overexpressed in gastric cancer and had potential diagnostic value [20]. These studies suggest that the development of cancer-related biomarkers may help predict patient prognosis and treatment strategies.

In recent years, miRNAs have obtained more and more attention for high diagnostic and/or prognostic significance in different human tumors, including gastric cancer [21-23]. Zhang et al. identified multiple miRNAs expression profiles and clinical information of gastric cancer patients, suggesting that a three-miRNA signature could play a role in predicting the prognosis of gastric cancer patients [24]. A study by Zheng et al. revealed that expression of miR-203 was downregulated in gastric cancer and that it might be a potential prognostic factor for gastric cancer [25]. The present study investigated expression of miR-106 in gastric cancer tissues and cell lines. Moreover, qRT-PCR results showed that expression of miR-106 was remarkably upregulated in gastric cancer tumor tissues and cell lines, indicating that miR-106 may be an oncogene in gastric cancer. Expression of miR-106 in gastric can-

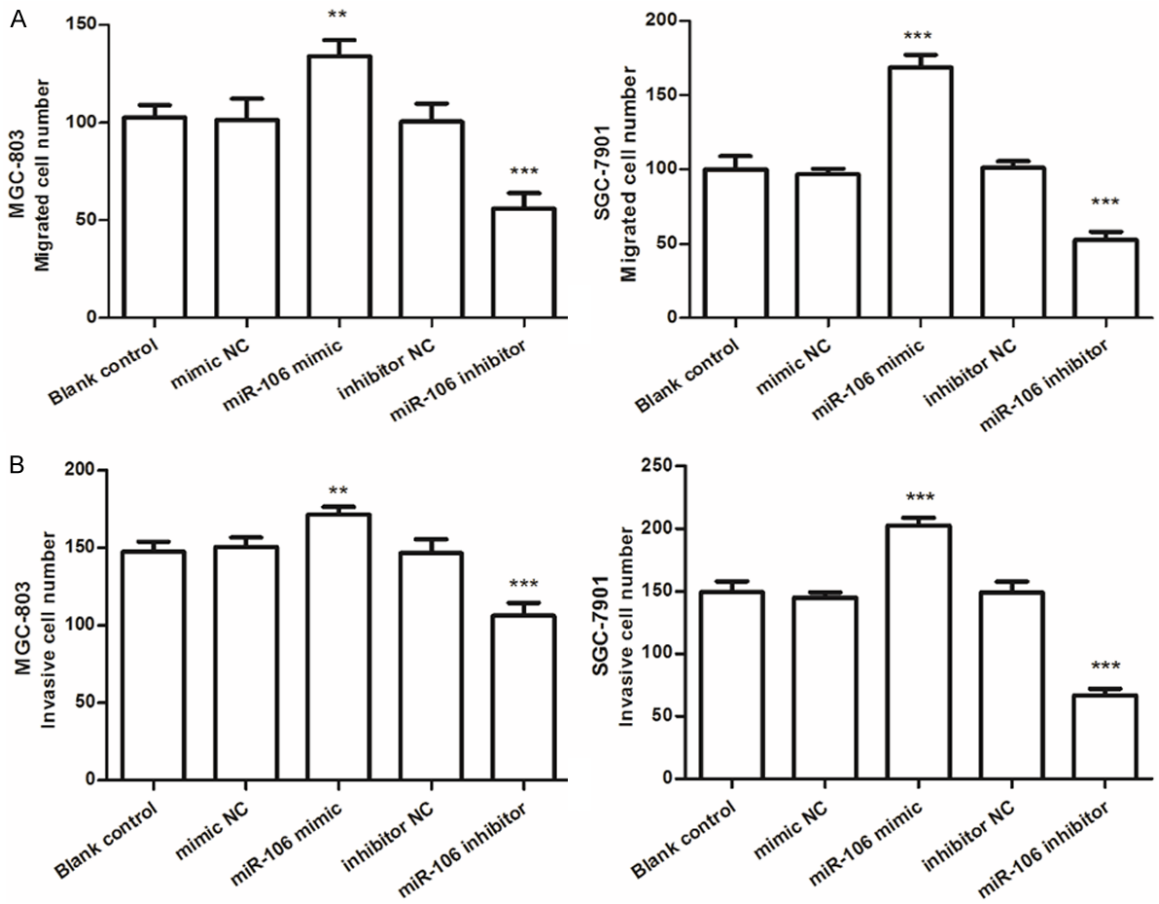

Figure 4. Results of migration and invasion analysis for MGC-803 and SGC-7901 cells. A, B. Overexpression of miR-106 by miR-106 mimic could promote the cell migration and invasion, but downregulated miR-106 expression could inhibit cell migration and invasion. (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$).

cer tumor tissues has shown consistent results within serum samples in previous studies [11, 12].

Further clinical-based analysis found that expression of miR-106 was significantly correlated with lymph node metastasis and TNM stage, suggesting that miR-106 is involved in the development of gastric cancer. Present results suggest the potential relationship between high miR-106 expression and unfavorable prognosis of tumors. To further evaluate the prognostic significance of miR-106 in gastric cancer, this study analyzed the relationship between miR-106 expression and overall survival of patients using Kaplan-Meier and Cox analyses. Kaplan-Meier analysis results showed that patients in the high miR-106 expression group had a shorter survival duration than those in the low miR-106 expression group. According to multivariate Cox regression analysis, miR-106 expression was significantly correlated with prognosis of gastric cancer, suggesting that it might be an independent prognostic marker in gastric cancer.

Increasing evidence has shown that miR-106 plays a crucial role in the progression of some malignancies [26-28]. A study by Yen et al. showed that miR-106b and its cluster, miR-93 and miR-25, are upregulated in HCC patients and that miR-106b promotes cancer progression in hepatitis B virus-associated HCC [26]. In colorectal cancer, miR-106 was identified to be upregulated in metastatic colorectal cancer, promoting cell migration and invasion by directly targeting DLC1 [27]. To explore the functional roles of miR-106 in the progression of gastric cancer, the effects of miR-106 on gastric cancer cell proliferation, migration, and invasion were investigated. In two gastric cancer cell lines, MGC-803 and SGC-7901, it was found

that overexpression of miR-106 by miR-106 mimics could promote cell proliferation, migration, and invasion, while downregulation of miR-106 by miR-106 inhibitors inhibited cell proliferation, migration, and invasion. Taken together, results suggest that miR-106 could promote the progression of gastric cancer. In a study of bladder cancer, miR-106 overexpression was found to significantly reverse the effects of BAI on proliferation, migration, and apoptosis of T24 cells, which suppressed proliferation and migration and induced apoptosis of T24 cells through downregulating miR-106, along with inhibition of the JNK and MEK/ERK pathways [29]. However, the detailed molecular mechanisms of miR-106 in gastric cancer require further investigation.

In conclusion, the current study demonstrates that miR-106 functions as an oncogene in gastric cancer that promotes cancer progression. Upregulated expression of miR-106 may serve as a candidate prognostic biomarker and a therapeutic target for gastric cancer patients.

Disclosure of conflict of interest

None.

Address correspondence to: Shihua Zhang, Department of Brain surgery, First Affiliated Hospital of Jiamusi University, No. 348, Dexiang Street, Jiamusi 154002, Heilongjiang, China. Tel: 0454-8623330; Fax: 0454-8623330; Email: fu26578249yi@163.com

References

[1] Ang TL and Fock KM. Clinical epidemiology of gastric cancer. Singapore Med J 2014; 55: 621-628.

[2] Niccolai E, Taddei A, Prisco D and Amedei A. Gastric cancer and the epoch of immunotherapy approaches. World J Gastroenterol 2015; 21: 5778-5793.

[3] Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Niksic M, Bonaventure A, Valkov M, Johnson CJ, Esteve J, Ogunbiyi OJ, Azevedo ESG, Chen WQ, Eser S, Engholm G, Stiller CA, Monnereau A, Woods RR, Visser O, Lim GH, Aitken J, Weir HK and Coleman MP. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 2018; 391: 1023-1075.

[4] Strong VE, Wu AW, Selby LV, Gonen M, Hsu M, Song KY, Park CH, Coit DG, Ji JF and Brennan MF. Differences in gastric cancer survival between the U.S. and China. J Surg Oncol 2015; 112: 31-37.

[5] Ameres SL and Zamore PD. Diversifying microRNA sequence and function. Nat Rev Mol Cell Biol 2013; 14: 475-488.

[6] Zhang Y, Zeng A, Liu S, Li R, Wang X, Yan W, Li H and You Y. Genome-wide identification of epithelial-mesenchymal transition-associated microRNAs reveals novel targets for glioblastoma therapy. Oncol Lett 2018; 15: 7625-7630.

[7] Mei LL, Qiu YT, Zhang B and Shi ZZ. MicroRNAs in esophageal squamous cell carcinoma: Potential biomarkers and therapeutic targets. Cancer Biomark 2017; 19: 1-9.

[8] Dan B, Luo J, Li K and Chen S. Prognostic Value of miR-375 for Survival Outcomes in Various Cancers: A Systematic Review and Meta-Analysis. Oncol Res Treat 2018; 41: 47-50.

[9] Mearini E, Poli G, Cochetti G, Boni A, Egidi MG and Brancorsini S. Expression of urinary miRNAs targeting NLRs inflammasomes in bladder cancer. Onco Targets Ther 2017; 10: 2665-2673.

[10] He T, McColl K, Sakre N, Chen Y, Wildey G and Dowlati A. Post-transcriptional regulation of PIAS3 expression by miR-18a in malignant mesothelioma. Molecular oncology 2018;

[11] Peng Q, Shen Y, Lin K, Zou L and Zhu Y. Comprehensive and integrative analysis identifies microRNA-106 as a novel non-invasive biomarker for detection of gastric cancer. J Transl Med 2018; 16: 127.

[12] Song J, Yin J, Bai Z, Zhang J, Meng H, Cai J, Deng W, Ma X and Zhang Z. The profile of serum microRNAs predicts prognosis for resected gastric cancer patients receiving platinum-based chemotherapy. Dig Dis Sci 2017; 62: 1223-1234.

[13] Gockel I and Hoffmeister A. Endoscopic or surgical resection for gastro-esophageal cancer. Dtsch Arztebl Int 2018; 115: 513-519.

[14] Cormedi MCV, Katayama MLH, Guindalini RSC, Faraj SF and Folgueira M. Survival and prognosis of young adults with gastric cancer. Clinics (Sao Paulo) 2018; 73: e651s.

[15] Katono K, Sato Y, Kobayashi M, Saito K, Nagashio R, Ryuge S, Igawa S, Nakashima H, Shiomi K, Satoh Y, Ichinoe M, Murakumo Y, Saegusa M and Masuda N. Clinicopathological significance of S100A14 expression in lung adenocarcinoma. Oncol Res Treat 2017; 40: 594-602.

[16] Zheng J, Cao F, Huang X, Ramen K, Xu X, Zhu Y, Chang W, Shan Y and Guo A. Eyes absent ho-

mologue 2 predicts a favorable prognosis in colorectal cancer. Onco Targets Ther 2018; 11: 4661-4671.
[17] Kim HJ, Kim LK, Lee SH, Park SA, Eoh KJ and Kim YT. Expression levels of the long noncoding RNA steroid receptor activator promote cell proliferation and invasion and predict patient prognosis in human cervical cancer. Oncol Lett 2018; 16: 5410-5418.
[18] Tolle A, Blobel CC and Jung K. Circulating miRNAs in blood and urine as diagnostic and prognostic biomarkers for bladder cancer: an update in 2017. Biomark Med 2018; 12: 667-676.
[19] Qi H and Wang Y. NOB1 gene as a potential biomarker in clinical outcomes and prognosis of patients with gastric cancer. Clin Lab 2018; 64: 1469-1475.
[20] Yoruker EE, Keskin M, Kulle CB, Holdenrieder S and Gezer U. Diagnostic and prognostic value of circulating lncRNA H19 in gastric cancer. Biomed Rep 2018; 9: 181-186.
[21] Yuan HL, Wang T and Zhang KH. MicroRNAs as potential biomarkers for diagnosis, therapy and prognosis of gastric cancer. Onco Targets Ther 2018; 11: 3891-3900.
[22] Harrandah AM, Mora RA and Chan EKL. Emerging microRNAs in cancer diagnosis, progression, and immune surveillance. Cancer Lett 2018; 438: 126-132.
[23] Chen L, Hu J, Pan L, Yin X, Wang Q and Chen H. Diagnostic and prognostic value of serum miR-99a expression in oral squamous cell carcinoma. Cancer Biomark 2018; 23: 333-339.
[24] Zhang C, Zhang CD, Ma MH and Dai DQ. Three-microRNA signature identified by bioinformatics analysis predicts prognosis of gastric cancer patients. World J Gastroenterol 2018; 24: 1206-1215.
[25] Zheng Y, Liu W, Guo L and Yang X. The expression level of miR-203 in patients with gastric cancer and its clinical significance. Pathol Res Pract 2017; 213: 1515-1518.
[26] Yen CS, Su ZR, Lee YP, Liu IT and Yen CJ. miR-106b promotes cancer progression in hepatitis B virus-associated hepatocellular carcinoma. World J Gastroenterol 2016; 22: 5183-5192.
[27] Zhang GJ, Li JS, Zhou H, Xiao HX, Li Y and Zhou T. MicroRNA-106b promotes colorectal cancer cell migration and invasion by directly targeting DLC1. J Exp Clin Cancer Res 2015; 34: 73.
[28] He QY, Wang GC, Zhang H, Tong DK, Ding C, Liu K, Ji F, Zhu X and Yang S. miR-106a-5p suppresses the proliferation, migration, and invasion of Osteosarcoma Cells by Targeting HMGA2. DNA Cell Biol 2016; 35: 506-520.
[29] Jiang L, Song H, Guo H, Wang C and Lu Z. Baicalein inhibits proliferation and migration of bladder cancer cell line T24 by down-regulation of microRNA-106. Biomed Pharmacother 2018; 107: 1583-1590.