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ABOUT COVER

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The primary aim of *World Journal of Gastrointestinal Oncology* (WJGO, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, etc.

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Basic Study

E3 ubiquitin ligase *TRIM55* promotes metastasis of gastric cancer cells by mediating epithelial-mesenchymal transition

Wei-Wei Li, Hao Yuan, Shuai Kong, Shu-Bo Tian

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Abstract

BACKGROUND

Gastric cancer (GC) is considered a major global health problem. The role of *TRIM55*, a member of the three-domain protein family, in GC is unknown.

AIM

To determine the expression of *TRIM55* in GC tissues and its relationship with clinicopathological characteristics, and to investigate the effects of *TRIM55* on the malignant biological behavior of GC cells.

METHODS

Differential expression of *TRIM55* in GC and para-cancer tissues was detected by immunohistochemistry, and the relationship between *TRIM55* level and clinicopathological characteristics and prognosis was analyzed. Gain-of-function, loss-of-function, cell counting kit-8 assay, colony formation, transwell assay, wound healing assay, and western blot analysis were used to assess the potential role of *TRIM55* in the development of GC.

RESULTS

TRIM55 expression was significantly increased in GC tissues compared with adjacent normal tissues. High expression of *TRIM55* was associated with advanced pathological stage and poor prognosis. Overexpression of *TRIM55* promoted invasion and metastasis of GC cells *in vitro* by regulating epithelial-mesenchymal transition (EMT), whereas knockdown of *TRIM55* had the opposite effect. Our data showed that *TRIM55* is highly expressed in GC tissues, and is associated with poor prognosis. *TRIM55* plays the role of an oncogene in GC, and it promotes metastasis of GC through the regulation of EMT.

CONCLUSION

TRIM55 may be a possible target for the diagnosis and prognosis of GC patients.

Key Words: *TRIM55*; Gastric cancer; Prognosis; Epithelial-mesenchymal transition

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Core Tip: *TRIM55* expression was elevated in gastric cancer (GC) cancer tissues. Depletion of *TRIM55* in GC cells suppressed proliferation, migration and invasion of cells. Knockdown of *TRIM55* affected the expression of cell epithelial-mesenchymal transition-related proteins. *TRIM55* may serve as an oncogene in GC.

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INTRODUCTION

Gastric cancer (GC) is one of the most common tumors and seriously affects patients' health[1]. Comprehensive treatment based on surgery is the preferred strategy for GC[2]. Postoperative metastasis is the leading cause of death from GC; however, the mechanisms underlying the occurrence and the development of GC have not been fully elucidated, and there is a lack of effective markers for early diagnosis[3]. Therefore, identifying molecular markers of GC is important for the early diagnosis, treatment, and prognostic evaluation of GC. The three-domain protein (TRIM) family is composed of many members, including the tripartite motif, which consists of a RING domain, 1 or 2 Box motifs, and a coiled-coil region[4]. Some TRIM proteins are involved in the regulation of cellular transcription, cell proliferation, and tumor development; thus, they play a role in either promoting or inhibiting cancer[5]. The structural diversity of TRIM family proteins underpins their functional diversity. *TRIM55*, also known as muscle-specific RING zinc finger protein 2, maintains muscle development and cardiac function. *TRIM55* plays an important role in early skeletal muscle differentiation and the generation of muscle fibers[6]. Studies have shown that mir-30-5p can inhibit muscle cell differentiation and regulate the alternative splicing of *TRIM55* by targeting Muscleblind-like Protein[7]. *TRIM55* can regulate the TNF- α -CCL2 pathway and promote an inflammatory response in the development of mesangial proliferative glomerulonephritis[8]; however, the role of *TRIM55* in GC has not been fully elucidated.

In this study, we determined the differential expression of *TRIM55* in GC patients and investigated the relationship between *TRIM55* and clinicopathological characteristics. We found that *TRIM55* induced proliferation, migration, and invasion of GC cells. We also investigated the mechanism underlying these effects.

MATERIALS AND METHODS

Tissue samples

Tissues were obtained from 91 GC patients admitted to the Department of Gastrointestinal Surgery of Shandong Provincial Hospital Affiliated to Shandong First Medical University between July 2014 and December 2015. The tumor tissue samples and adjacent normal gastric mucosal tissue samples were validated by pathologists. Of the 91 patients, 61 were male and 30 were female, with an average age of 63.6 years. Data such as gender and age of the patient, tumor location, tumor pathological stage, and lymph node metastasis, were also collected. In addition, five fresh GC tissue samples and matched

adjacent normal gastric tissues were obtained from our hospital. The research protocols were approved by the Ethics Committee of the Provincial Hospital Affiliated to Shandong First Medical University, and all the patients signed an informed consent form before surgery.

Cell culture and transfection

Human GC cell lines (AGS, MKN28, MGC803, SGC7901, HGC27, and MKN45) and the immortalized gastric mucosa cell line (GES-1) were provided by the Cell Center of the Chinese Academy of Medical Sciences. All the cell lines were cultured in RPMI-1640 medium containing 10% fetal bovine serum (FBS, Gibco, United States). Cells were cultured in an incubator at 37 °C and 5% CO₂. According to the CDS coding sequence of *TRIM55*, small interfering RNAs (siRNA) to knock down *TRIM55* were designed and synthesized by RiboBio (Guangzhou, China), and the scramble nonsense sequence was used as the negative control (si-control). The targeting *TRIM55* siRNA sequence was as follows: *TRIM55* siRNA, 5'-AUCAAACUUCUCACAAAGCUC-3'. The control siRNA was not homologous to any human genome sequence. For the overexpression assay, the coding sequence of *TRIM55* was amplified and cloned into a pcDNA3.1-HA vector to construct the *TRIM55* overexpression system (*TRIM55* plasmid). The pcDNA3.1-HA empty vector was used as the negative control in HGC27 cells.

Immunohistochemical staining

The GC tissue and adjacent tissue were embedded in paraffin and sliced into 4-μm-thick sections. Xylene was used for dewaxing and citrate buffer was used for antigen repair. After washing with PBS 4 times, the samples were sealed with BSA blocking solution at 37 °C. *TRIM55* primary antibody (Novus, United States) was added and incubated overnight at 4 °C. According to the instructions of the immunohistochemical test kit, the secondary antibody was added and incubated for 20 min at room temperature. Then, streptavidin-peroxidase conjugate was added and the samples were incubated for 20 min. DAB was used for staining and hematoxylin was used for redyeing and dehydration. The sections were observed and photographed under a microscope and analyzed with Image analysis software. According to the staining intensity, no staining was scored as 0, light yellow was scored as 1, brownish yellow was scored as 2, and brown was scored as 3. According to the percentage of positive cells, the score for no positive cells was 0, 1%–10% was 1, 11%–50% was 2, 51–75% was 3, and 76%–100% was 4. The expression of *TRIM55* was considered to be high if the multiple of the two scores was ≥ 5.

Quantitative real-time polymerase chain reaction

Total RNA was extracted using TRIzol reagent (Invitrogen) and reverse transcribed to cDNA using a reverse transcription kit (Takara, Dalian, China) following the manufacturer's instructions. The quantitative real-time polymerase chain reaction three-step method was used, and the 2^{-ΔΔCt} method was used to calculate the relative expression levels of *TRIM55*. GAPDH was used as the endogenous control. The upstream primer sequence of *TRIM55* was 5'-GGTTTGGATAGACATGGGGT-3', and the downstream primer sequence was 5'-TTCTCCTCTTGGGTTCGGGT-3'.

Cell counting kit-8 assay

Cells were seeded in 96-well plates (2000 cells/well) and placed into an incubator for further culture. Ten microliters of cell counting kit-8 (CCK-8) reagent (Dojindo, Mashikimachi, Japan) was added to each well on days 1, 2, 3, and 4. After 4 h incubation, the absorbance value at 450 nm (OD450) was measured with a microplate reader. The growth curve of cells was drawn according to the OD value. Three independent assays were performed for each time point.

Colony formation assay

Two thousand cells/well were plated in a six-well plate and allowed to grow in complete growth medium for 14 d. The colonies were then fixed with 4% paraformaldehyde for 15 min, followed by staining with 0.1% crystal violet solution for 10 min. The number of colonies was counted, and the average value was calculated from three independent experiments.

Transwell migration and invasion assay

GC cells at the logarithmic growth stage were trypsinized and suspended in serum-free media at a concentration of 1 × 10⁶ cells/mL. Two hundred microliters of the cell suspension was added to the upper transwell chamber. Culture medium containing 10% FBS was added to the lower chamber. For the invasion assay, the transwell membrane was coated with Matrigel. After 48 h incubation, the cells that did not pass through the membrane in the upper chamber were removed with cotton swabs. The migrated/invaded cells were fixed with paraformaldehyde for 30 min and stained with 0.1% crystal violet solution. The cells were observed under a microscope and five random fields were selected to count the number of migrated or invaded cells.

Wound healing assay

GC cells were inoculated into a six-well plate at a density of 5 × 10⁵ cells/well until 90% confluence was reached. Then, a sterile 100-μL pipette tip was used to scrape the bottom surface of the plate to form a

wound vertically. The cells were washed with $1\times$ PBS, and complete growth medium was added. The wound margins were observed at 0 and 24 h in 5 randomly selected microscopic regions, and the mean cell spacing was calculated.

Western blot assays

GC cells were collected and lysed in immunoprecipitation lysis buffer. After protein quantification by the BCA method, 30 μ g of protein sample was used for electrophoresis. After transfer and blocking, the membrane was incubated overnight at 4 °C with the primary antibody. Horseradish peroxidase-labeled secondary antibody was added and incubated for 1 h. The bands were visualized using chemiluminescence reagent.

Statistical analysis

Statistical analyses were performed using GraphPad Prism software version 7.0 (CA, United States). All the data are represented as mean \pm SD from three independent experiments. Differences among groups were compared using student's t-test and one-way analysis of variance. The prognostic factors were analyzed by univariate and multivariate Cox regression models. The Kaplan-Meier method was used to calculate the survival rate, and the log-rank test was used to compare different survival curves. A value of $P < 0.05$ was considered to indicate a statistically significant difference.

RESULTS

TRIM55 is highly expressed in GC samples

Immunohistochemical results showed that *TRIM55* was mainly expressed in the nucleus. **Figure 1A-D** shows the representative immunohistochemical staining images of *TRIM55* in normal gastric mucosa tissue and cancer tissue. The expression of *TRIM55* was significantly high in 91 GC tissues and low in para-cancer tissues (**Table 1**, $P < 0.001$). There was no significant correlation between *TRIM55* expression and age at diagnosis, gender, tumor location, or Lauren type ($P > 0.05$, **Table 2**). However, a significant relationship was found between *TRIM55* expression and tumor stage, lymph node metastasis, and T stage ($P < 0.05$, **Table 2**).

To further confirm the results, we performed western blotting using five GC specimens and matched normal tissues. The results showed that protein levels of *TRIM55* in GC tissues were up-regulated compared to non-tumor tissues (**Figure 1E**).

Relationship between TRIM55 expression and prognosis of GC

The 5-year survival rate of patients with high *TRIM55* expression was lower than that of those with low expression ($P = 0.026$, **Figure 1F**). The median overall survival of patients with high and low expression of *TRIM55* was 34 mo [95% confidence interval (CI): 13.3–62.8] and 57 mo (95%CI: 25.5–84.5), respectively. Similarly, patients with high *TRIM55* gene expression had a poor prognosis in the TCGA database (**Figure 1G**). Univariate Cox regression analysis showed that T stage, lymph node metastasis, TNM stage, and *TRIM55* expression level were the influencing factors for the prognosis of GC patients (**Table 3**). Further multivariate Cox regression analysis showed that lymph node metastasis, TNM stage, and *TRIM55* expression level were independent factors affecting the prognosis of GC (**Table 3**).

TRIM55 protein is upregulated in GC cell lines

The protein level of *TRIM55* was analyzed in the immortalized gastric mucosal epithelial cell line GES-1 and six GC cell lines (AGS, MKN28, MGC803, SGC7901, HGC27, and MKN45). The results showed that the expression level of *TRIM55* in GC cell lines was significantly higher than that in GES-1 cells (**Figure 2A**). Among them, the expression level of *TRIM55* was highest in SGC7901 and lowest in the HGC27 cell line.

Transfection efficiency of TRIM55 siRNA and TRIM55 overexpressed plasmid

To analyze the effects of *TRIM55* knockdown, SGC7901 (cells with high *TRIM55* expression) GC cells were transfected with *TRIM55* siRNA. The results showed that both mRNA and protein expressions of *TRIM55* were significantly lower in cells transfected with *TRIM55* siRNA compared to those in the control group (**Figure 2B** and **C**). HGC27 cells with low endogenous *TRIM55* expression were transfected with *TRIM55* overexpressed plasmid to determine the effects. We found that cells transfected with the overexpressed plasmid had higher mRNA and protein levels of *TRIM55* compared to those transfected with the empty vector (**Figure 2D** and **E**).

TRIM55 promotes proliferation of GC cells

The CCK-8 assay was used to determine the proliferation of GC cells. The results showed that SGC7901 cell proliferation was significantly inhibited on days 2, 3, and 4 after *TRIM55* knockdown ($P < 0.001$, **Figure 3A**). However, the proliferation of HGC27 cells was significantly increased on days 2, 3, and 4 (P

Table 1 Immunohistochemical expression of *TRIM55* in gastric cancer and normal tissues

Tissue	N	High expression	Low expression	P value
Gastric cancer	91	40	51	< 0.001
Normal	91	3	89	

Table 2 Association between *TRIM55* expression and clinicopathological characteristics

Variables	No. of case	TRIM55 expression		χ^2	P value
		High (n = 40)	Low (n = 51)		
Gender				0.284	0.594
Male	61	28	33		
Female	30	12	18		
Age (n)				0.216	0.642
≤ 65	48	20	28		
> 65	43	20	23		
Tumor location				0.008	0.928
Proximal	14	6	8		
Dismatal	77	34	43		
pT stage				6.232	0.013
T1 + T2	43	13	30		
T3 + T4	48	27	21		
Lymph node metastasis				5.506	0.019
Negative	49	16	33		
Positive	42	24	18		
TNM stage				5.146	0.023
I + II	53	18	35		
III	38	22	16		
Lauren histotype				3.366	0.067
Intestinal	47	25	22		
Diffuse	44	15	29		

< 0.001, **Figure 3B**) when *TRIM55* was overexpressed in these cells. These results suggest that *TRIM55* can promote the proliferation of GC cells.

The colony formation assay showed that the colony number was significantly reduced after siRNA transfection in SGC7901 cells (**Figure 3C**). Similarly, overexpression of *TRIM55* in HGC27 cells enhanced the ability of cells to form colonies (**Figure 3D**).

TRIM55 promotes invasion and migration of GC cells

The transwell migration and invasion assay results showed that *TRIM55* knockdown significantly reduced the migration and invasion of SGC7901 cells (**Figure 4A**). Furthermore, the number of migrated and invaded HGC27 cells was significantly increased after *TRIM55* overexpression (**Figure 4B**). The wound-healing assay revealed that knockdown of *TRIM55* significantly impaired the migration ability of SGC7901 cells (**Figure 5A**), while HGC27 migration ability was enhanced after overexpression of *TRIM55* (**Figure 5B**). These results suggest that *TRIM55* could promote the invasion and migration of GC cells.

TRIM55 promotes the migration and invasive growth of GC cells by inducing epithelial-mesenchymal transition

To further explore the potential mechanism of how *TRIM55* promotes the progression of GC, we

Table 3 Univariate and multivariate Cox regression models for estimating the overall survival

Variable	Univariate analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Gender	0.79	0.12–1.38	0.463			
Age	0.56	0.38–1.50	0.517			
Tumor location	1.67	0.53–2.27	0.770			
pT stage	0.85	0.61–0.93	0.041			
Lymph node metastasis	3.29	2.07–5.44	0.005	2.64	1.35–3.08	0.021
TNM stage	2.18	1.32–2.89	0.016	1.20	1.06–1.88	0.028
Lauren histotype	1.45	0.39–2.46	0.433			
TRIM55	2.37	1.53–3.81	0.028	1.48	1.17–1.92	0.035

HR: Hazard ratio; CI: Confidence interval.

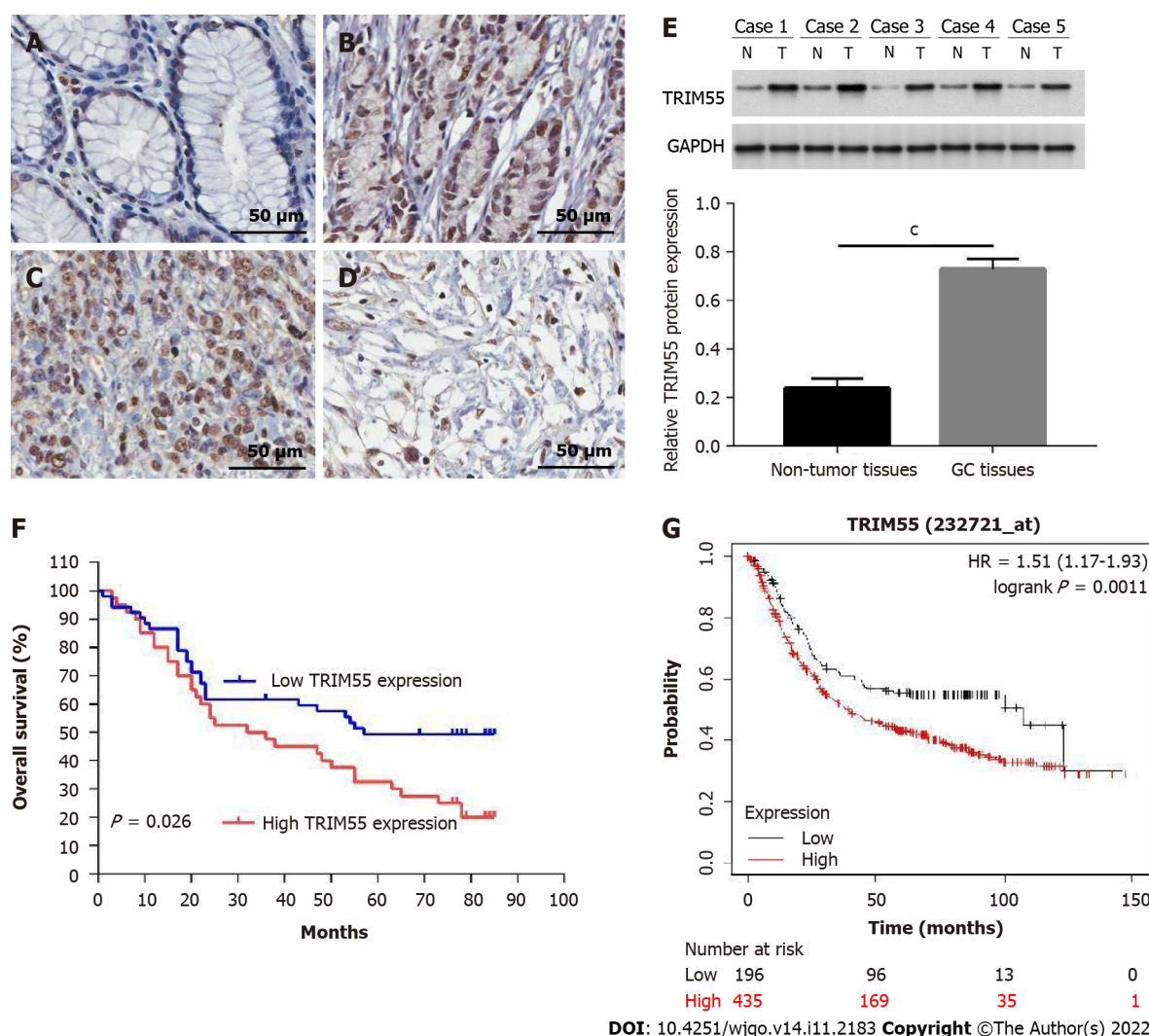


Figure 1 Representative images of immunohistochemical staining for TRIM55 in human gastric cancer tissue and its prognostic significance. A: Low expression of TRIM55 in gastric normal mucosa tissue; B: TRIM55 expression in well-differentiated adenocarcinoma; C: TRIM55 expression in poorly differentiated adenocarcinoma; D: Overexpression of TRIM55 in signet-ring cell carcinoma. Original magnification, 400 ×; E: TRIM55 protein levels in five tumor samples and their matched normal tissues; F: Overall survival curves for 91 gastric cancer (GC) patients according to TRIM55 protein expression ($P = 0.026$); G: Overall survival curves of TCGA GC patients with different TRIM55 expression. $P < 0.001$. HR: Hazard ratio; GC: Gastric cancer.

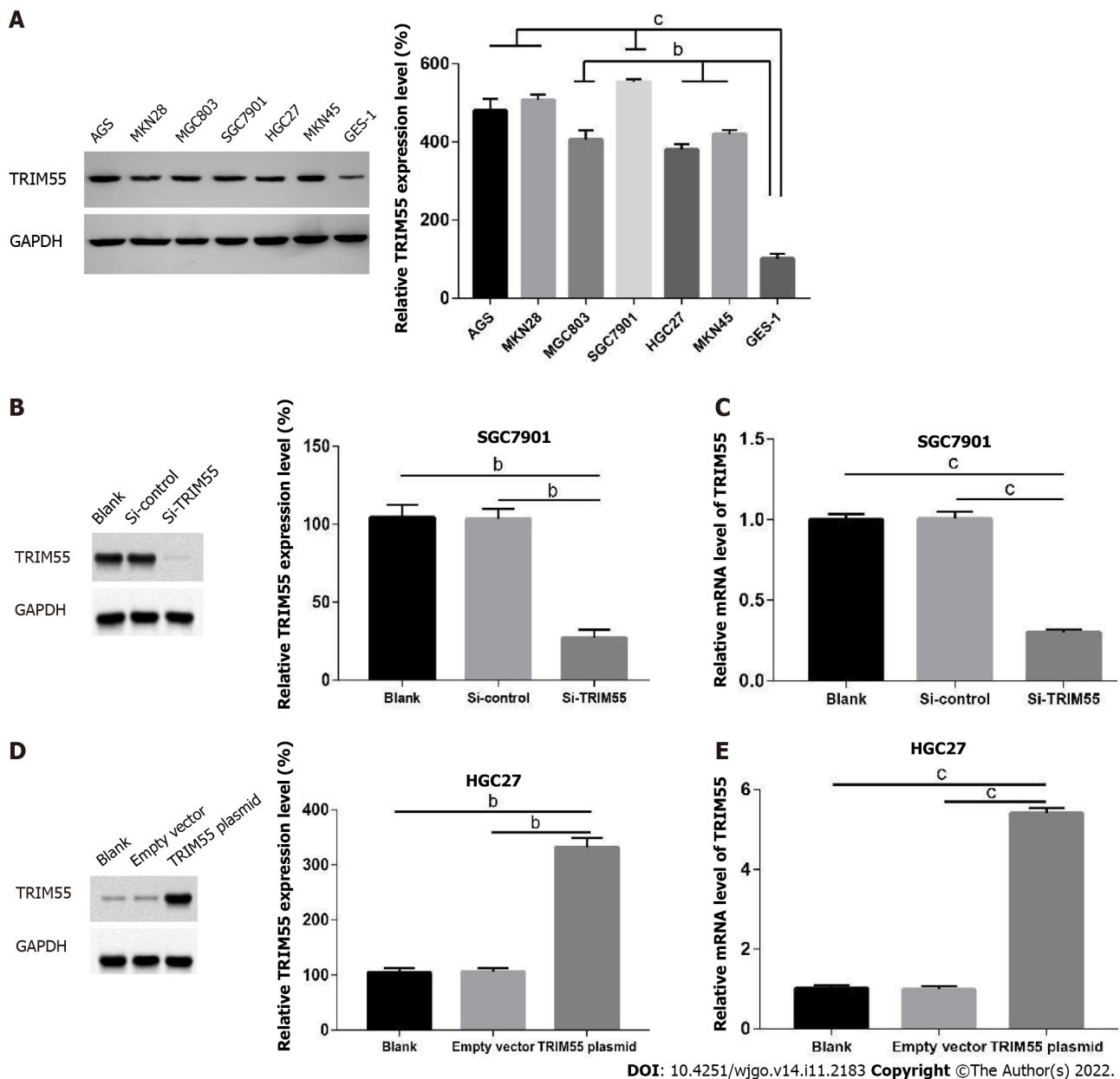
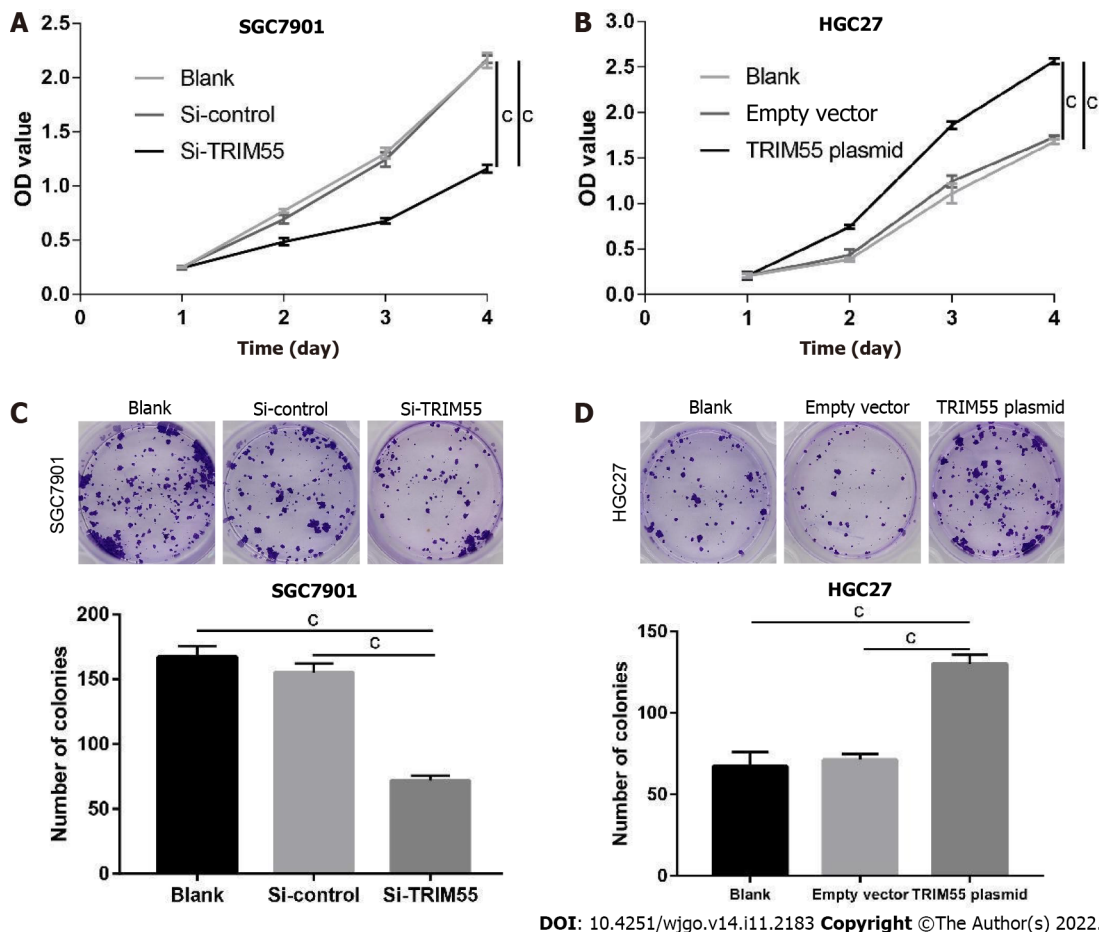


Figure 2 *TRIM55* expression in gastric cancer cells. A: The expression of TRIM protein was detected in gastric cancer (GC) cells by western blot. The histogram shows the expression of *TRIM55* in GC cells was stronger than that in gastric mucosa cell line; B: The interference efficiency of *TRIM55* small interfering RNA (siRNA) in SGC7901 cells was detected by Western blot; C: Quantitative real-time-polymerase chain reaction assay was performed to determine *TRIM55* expression after transfection with siRNA; D: The up-regulation of *TRIM55* expression in HGC27 cells was detected by Western blot; E: *TRIM55* mRNA expression level in HGC27 after transfection with the *TRIM55* plasmid. ^b*P* < 0.01; ^c*P* < 0.001.

analyzed the expression of epithelial-mesenchymal transition (EMT)-related proteins by western blot analysis (Figure 6). The results showed that in the SGC7901 cell line, E-cadherin expression was significantly up-regulated after *TRIM55* knockdown, while N-cadherin, Vimentin, ZEB1, and Snail expression were significantly down-regulated compared with the control group (Figure 6A). Furthermore, the opposite results were observed when *TRIM55* was overexpressed in the HGC27 cell line (Figure 6B). These results confirmed that *TRIM55* promotes the invasion and metastasis of GC cells by inducing EMT.

DISCUSSION

TRIM55 belongs to the TRIM protein family, which plays an important role in the development and progression of tumors. TRIM proteins have three characteristic domains and function as an E3 ligase; they also mediate ubiquitination and regulate intracellular pathophysiological and tumor-related processes by degrading target molecules. TRIM family members exhibit oncogenic and tumor-



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Figure 3 *TRIM55* regulates gastric cancer cell proliferation. A and B: Cell viability detected by cell counting kit-8 assay in SGC7901 cells after knockdown of *TRIM55* and in HGC27 cells after overexpression of *TRIM55*; C and D: Colony formation analysis of *TRIM55* knockdown-treated SGC7901 cells and *TRIM55* overexpression-treated HGC27 cells. $^*P < 0.001$.

suppressive capacities in different human cancer types by regulating signal transduction pathways[9, 10]. EMT is a transitional process in which epithelial cells lose intercellular adhesion and polarity, and they acquire mesenchymal cell characteristics, enhanced cell motility, and migration ability[11,12].

The progression of EMT is regulated by translational factors and epigenetic modification[13]. Also, microRNAs and long non-coding RNAs are also involved in EMT regulation as post-translational regulators[14]. The tumor cells or other stromal cells can secrete exosomes. Exosomes are extracellular vesicles with a lipid bilayer containing proteins, lipids and functional RNAs, which can transfer information between tumor cells or between tumor cells and the tumor microenvironment, thereby regulating the EMT process[15,16]. As EMT plays essential physiological roles, EMT-targeted therapy combined with conventional chemotherapy can improve the sensitivity of tumor cells to drugs.

TRIM proteins were found to be associated with EMT in various types of cancer. TRIM11 protein was upregulated in GC tissue and cell lines, and it could promote cell proliferation, migration, invasion, and EMT of GC by activating β -catenin signaling[17]. TRIM47 mainly influenced the EMT signaling pathway, was highly expressed in GC, and was associated with poor prognosis of patients[18]. In GC, *TRIM44* expression was also increased in GC tissues and cell lines, and it regulated GC cell metastasis by altering the expression of EMT-associated factors[19].

Previous studies have demonstrated that the role of *TRIM55* in tumors is tissue specific. For example, a study revealed that *TRIM55* expression was significantly suppressed in lung adenocarcinoma tissues and tumor cells. *TRIM55* exerted its tumor-suppressive effect by increasing the degradation of Snail protein *via* ubiquitination[20]. *TRIM55* was downregulated in hepatocellular carcinoma (HCC) tissue and associated with tumor stage and poor prognosis. Overexpression of *TRIM55* can suppress the migration and invasion of HCC cells through EMT and the MMP2 pathways[21].

To the best of our knowledge, our study is the first to determine the expression levels and biological functions of *TRIM55* in GC. We demonstrated that *TRIM55* could be a potential new biomarker for diagnosing and evaluating GC patients. First, we performed immunohistochemical staining, and the results showed that *TRIM55* was highly expressed in GC tissues and that *TRIM55* expression was related to the T stage, lymph node metastasis, and TNM stage of GC. Survival analysis showed that the 5-year survival rate of GC patients with high expression of *TRIM55* was significantly reduced. Cox

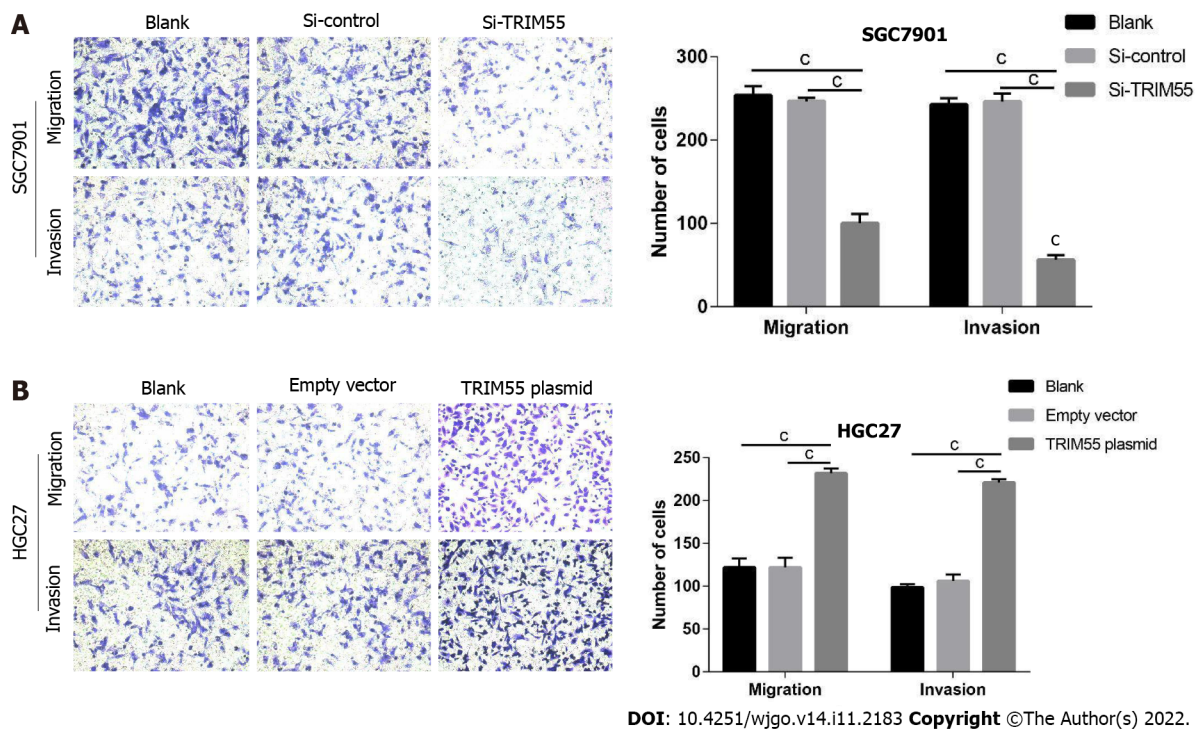


Figure 4 *TRIM55* promotes metastasis of gastric cancer cells. A: Migration and invasion analysis of *TRIM55* knockdown-treated SGC7901 cells; B: Migration and invasion analysis of *TRIM55* overexpression treated-HGC27 cells. $^*P < 0.001$.

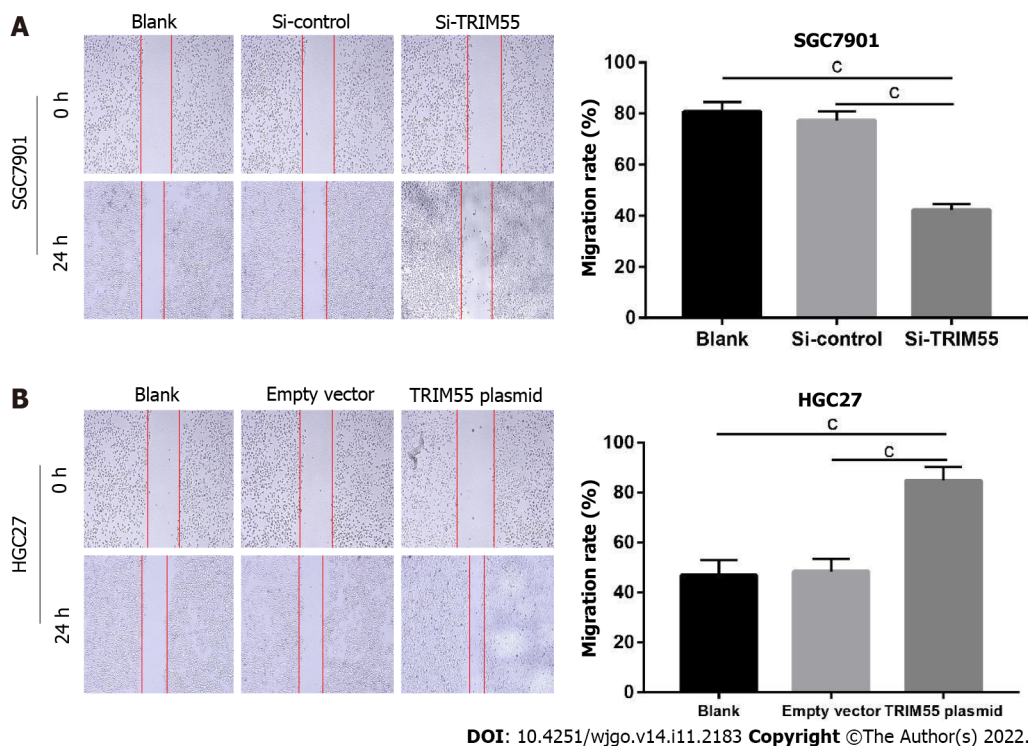


Figure 5 Wound healing assays were performed in gastric cancer cells. A: Migration rates of SGC7901 cells at 24 h were lower than that in control groups after knockdown of *TRIM55*; B: Migration rates of HGC27 cells at 24 h were higher than that in control groups after overexpression of *TRIM55*. $^*P < 0.001$.

regression analysis also confirmed that *TRIM55* expression was an independent prognostic factor in GC. These results suggest that *TRIM55* may be involved in the occurrence and development of GC. Furthermore, to confirm the biological functions of *TRIM55* in GC, we performed a gain and loss of function experiment *in vitro*. Results from the CCK-8 assay, colony formation assay, transwell, and wound healing assays indicated that inhibition of *TRIM55* decreases the proliferation and invasion of GC cells, whereas the overexpression of *TRIM55* promotes these processes in GC cells. Finally, we used

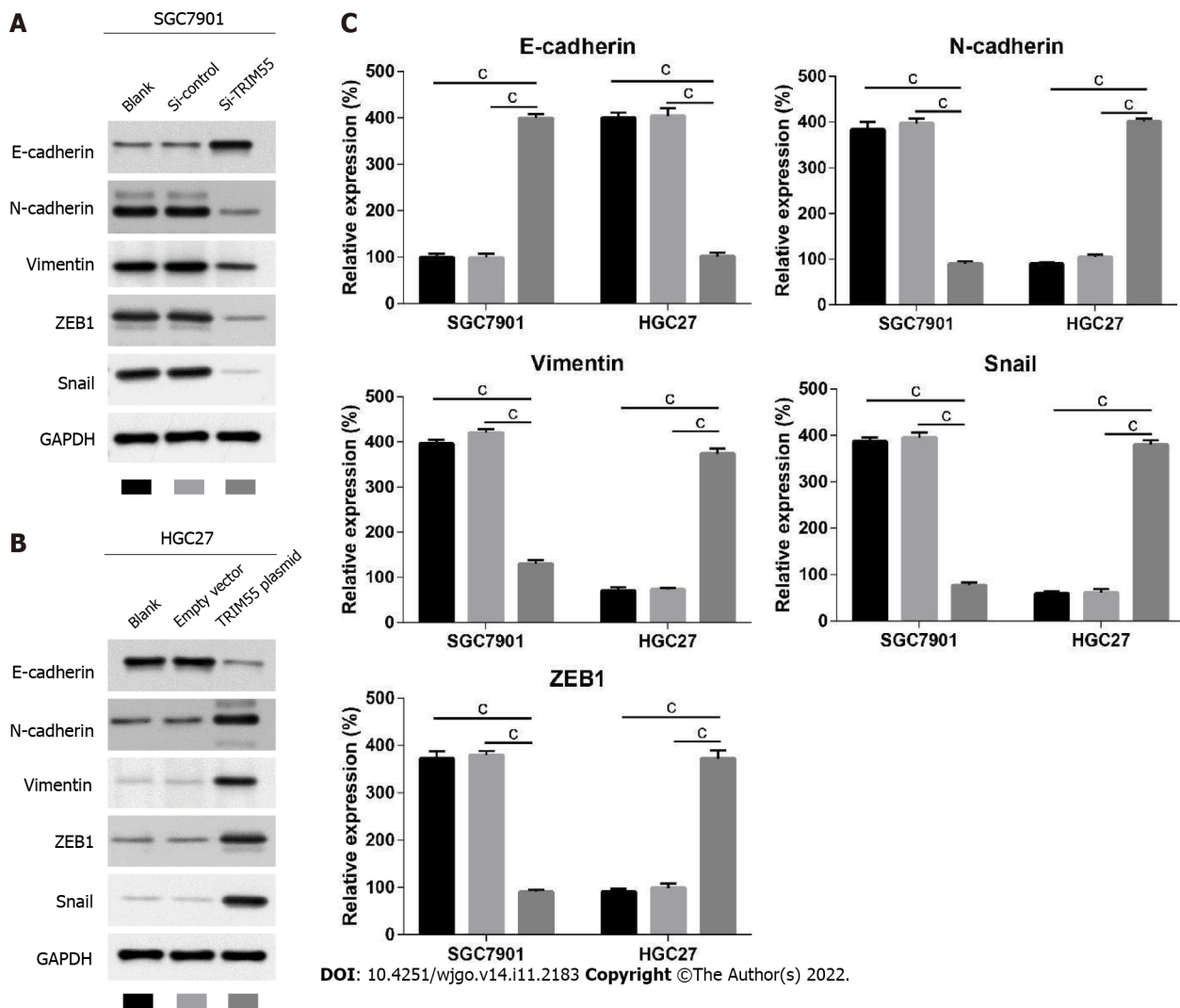


Figure 6 Western blot results of epithelial-mesenchymal transition pathway-related proteins in gastric cancer cells. A and B: Western blot analysis of E-cadherin, N-cadherin, Vimentin, ZEB1, and Snail after *TRIM55* knockdown and overexpression in SGC7901 and HGC27 cells; C: Histogram of the expression of E-cadherin, N-cadherin, Vimentin, Snail, and ZEB1 proteins related to metastasis after knockdown or overexpression of *TRIM55*. $^{\circ}P < 0.001$.

western blot analysis to confirm that knockdown or overexpression of *TRIM55* could alter the EMT-related protein, suggesting that *TRIM55* could regulate the EMT process. TRIM proteins could serve the ubiquitination function to stabilize or dislocate target proteins in various cellular compartments[4]. Ubiquitination is a post-transcriptional modification that labels the target proteins to be degraded at the proteasome level. Thus, TRIM family members determine both tumor suppressor and oncogenic roles by affecting the signal pathways in cancer development and progression. For example, TRIM29 and TRIM8 exhibited contextual function in different cancers[22-24]. They negatively or positively regulate tumorigenesis and tumor progression by affecting pathways. In our study, we showed that *TRIM55* is highly expressed in gastric tumors and cultured tumor cells. *TRIM55* has E3 ubiquitin ligase activity and whether it can regulate the EMT-related proteins through ubiquitination requires further investigation.

However, some limitations exist in our study. First, the detection of *TRIM55* was based on a single-center clinical cohort, and the functional experiments were only performed *in vitro*. Future studies should enroll more patients and utilize animal models to confirm our conclusions. Second, *TRIM55* has E3 ubiquitin ligase activity and whether it can regulate the EMT-related proteins through ubiquitination requires further study.

CONCLUSION

In summary, our study analyzed the expression of *TRIM55* in GC and demonstrated that *TRIM55* could promote GC cell proliferation, migration, and invasion *via* the EMT process. Overexpression of *TRIM55* could be an independent factor predicting poor survival, and *TRIM55* may serve as a potential therapeutic target for GC. In addition, whether *TRIM55* can affect EMT through other molecular

mechanisms remains to be examined in future studies.

ARTICLE HIGHLIGHTS

Research background

TRIM55 plays important role in hepatocellular carcinoma and lung adenocarcinoma. However, little is known about the role of *TRIM55* in gastric cancer (GC).

Research motivation

To discover the targets for the diagnosis, treatment and prognosis prediction of GC.

Research objectives

To explore the biological function of *TRIM55* and its underlying molecular mechanism in GC.

Research methods

The expression of *TRIM55* was determined by quantitative real-time polymerase chain reaction and Western blot. Cell counting kit-8 assay, colony formation, wound healing assay and transwell assay were used to investigate the *TRIM55* function.

Research results

TRIM55 expression levels were significantly increased in GC cell lines and tissues. High expression of *TRIM55* was correlated with poor prognosis of GC patients. Knockdown of *TRIM55* in GC cell lines inhibited proliferation, colony formation, migration and invasion in vitro. *TRIM55* can regulate the expression of epithelial-mesenchymal transition-related proteins in GC cells.

Research conclusions

TRIM55 functions as an oncogene through promoting cell proliferation, migration and invasion in GC.

Research perspectives

TRIM55 may be a new potential target in GC treatment.

FOOTNOTES

Author contributions: Li WW and Yuan H contributed equally to this work; Tian SB and Li WW designed the study; Li WW and Yuan H performed all experiments; Kong S and Tian SB analyzed the data and drafted the article; All authors read and approved the final manuscript.

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Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at ttkl_bo@126.com.

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