Original Article

MiR-873-5p targets THUMPD1 to inhibit gastric cancer cell behavior and chemoresistance

Qinggui Chen[1#], Li Lin[2#], Boliang Xiong[3#], Wensheng Yang[4], Junli Huang[5], Huibo Shi[6,7], Zhenfa Wang[2]

[1]Department of General Surgery, Zhongshan Hospital, Xiamen University, Xiamen, China; [2]Department of Gastrointestinal Surgery, Zhongshan Hospital, Xiamen University, Xiamen, China; [3]Department of Radiotherapy, Zhongshan Hospital, Xiamen University, Xiamen, China; [4]Department of Pathology, Chenggong Hospital, Xiamen University, Xiamen, China; [5]Department of General Surgery, Chenggong Hospital, Xiamen University, Xiamen, China; [6]Institute of Organ Transplantation, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [7]Key Laboratory of Organ Transplantation, Ministry of Education NHC Key Laboratory of Organ Transplantation, Wuhan, China

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[#]These authors contributed equally to this work and should be regarded as co-first authors.

Correspondence to: Zhenfa Wang. 201-209 Hubin South Road, Siming District, Xiamen 361004, China. Email: 13806062519@139.com; Huibo Shi. Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, China. Email: jimshihuihuibo@163.com.

Background: Gastric cancer is one of the most common gastrointestinal tumors. Evidence has pointed to the fact that miRNAs play critical roles in the occurrence, development, and metastasis of gastric cancer by regulating cell proliferation, differentiation, apoptosis, and invasion.

Methods: In this study, first the relationship of miR-873-5p level and tissues types/LN(+/-)/metastasis(+/-)/tumor size was analysis, respectively. Second, the CCK8 and Transwell assay was used to determine the proliferation, invasion and migration of GC cells transfected with overexpression-/low expression-miR-873-5p. Third, the cell viability were analysis in the GC cells transfected with overexpression-/low expression-miR-873-5p treatment with different chemotherapy drugs. Fourth, the target gene of miR-873-5p was predicted using bioinformation methods. Fifth, the relationship of miR-873-5p with target gene-THUMPD1 were explored by using Wb and luciferase activity assay, *et al.*

Results: We confirmed that miR-873-5p was negatively correlated with GC including tumor size, LN metastasis, distant metastasis. The miR-873-5p enhanced the sensitivity of Doxorubicin/Fluorouracil and cisplatin. The THUMPD1 was the target gene of miR-873-5p. Moreover, miR-873-5p could target the THUMPD1 axis so as to inhibit gastric cancer cell behavior as well as chemoresistance.

Conclusions: MiR-873-5p plays a role in regulating cell behavior as well as regulating chemoresistance in gastric cancer. In addition, THUMPD1, as a downstream molecule of miR-873-5p, plays an important role in the cell behavior and chemoresistance of gastric cancer. The research first confirmed that miR-873-5p could inhibit gastric cancer cell behavior and chemoresistance by targeting the THUMPD1.

Keywords: Gastric cancer; miR-873-5p; quantitative real-time polymerase chain reaction (qRT-PCR); Western blot

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Introduction

Gastric cancer is one of the foremost common gastrointestinal tumors. Although the incidence rate has declined in recent years, the incidence and fatality rate still account for 8% and 10% of systemic malignancies worldwide, respectively, and most of the new cases and deaths are concentrated in East Asia and developing countries (1). In China, the incidence of gastric cancer ranks second among males and fourth among females (2). In 2017, nearly 562,000 people died of gastric cancer (3). Early diagnosis of gastric cancer is an important means to improve the treatment effect of gastric cancer and improve the prognosis of patients. Statistics show that if the disease is confined to the mucosa and submucosa in the early stage of gastric cancer treatment, the 5-year survival rate of patients can reach more than 90% (4). However, even in developed countries, more than 50% of diagnosed patients have entered the advanced stage of the disease, and the probability that the lesion and metastasis can be completely removed by surgery is less than 50% (5). The reason is that the early symptoms of gastric cancer are hidden. As the most important diagnostic method for gastric cancer, achieving large-scale screening with gastroscopy is difficult. Moreover, gastroscopy has limitations in the diagnosis of precancerous lesions and early cancer (6).

In recent years, more studies have focused on the relationship between microRNAs (miRNAs) and gastric cancer. It is currently believed that miRNAs can participate in the occurrence, development, and metastasis of tumors by regulating cell proliferation, differentiation, apoptosis, and invasion (7,8). Abnormal expression of miRNAs may lead to carcinogenic or tumor-suppressive effects in cancer, which mainly depends on the tumor type and their target genes (9). MiRNAs can also be used as oncogenes or tumor suppressor genes to promote or suppress gastric cancer development (10). For example, the expression of miR-191 in gastric cancer tissues was significantly higher than that in normal tissues, and 9 possible target genes were detected. These results suggest that miR-191 can promote the malignant transformation of gastric mucosal cells by inhibiting the expression of these genes (11). MiR-23a is up-regulated in gastric cancer. The protein content of IL-6R, which is the target of miR-23a, is negatively correlated with miR-23a. The above results indicate that miR-23a promotes the growth of gastric cancer cells by acting with IL-6R (12). Furthermore, previous studies confirmed that miR-206 can inhibit the expression of CyclinD2 in rhabdomyosarcoma, thereby inhibiting the occurrence of tumors (13). MiR-873-5p was first found in the hippocampus of temporal lobe epileptic rats with memory impairment (14). MiR-873-5p targets HMOX1 to regulate its expression and inhibit neuronal cell apoptosis to play a protective role (15). Meanwhile, in renal injury induced by an adhesion protein, METTL3/m6A/miRNA-873-5p plays a protective role by regulating the Keapl/NrG pathway to reduce oxidative stress and apoptosis (16). In lung cancer, miR-873-5p is the downstream target gene of lncRNA DCGR5 to regulate the expression of TUSC3. Therefore, miR-873-5p plays an important role in tumor progression (17). However, the detailed information is still poor on the expression and biological function of miR-873-5p in gastric cancer. THUMPD1 is specific adaptor protein that modulates tRNA acetylation by interacting with NAT10 which is a biomarker in some cancer types (18). Previous studies had show that THUMPD1 might interact with cancer progression and invasion, such as colon cancer, breast cancer, hepatocellular cancer, etc. (19-21).

And in our study, we also predict that the target gene of miR-873-5p is THUMPD1. So our study is the first to detect the expression of miR-873-5p in both clinical patients and cell lines of gastric cancer. Then, the functional roles of miR-873-5p in the cell lines were further studied. In addition, we explored not only the detailed molecular mechanisms of miR-873-5p but also the detailed molecular mechanisms of THUMPD1. Therefore, this study may provide the basis for further relevant studies targeting gastric cancer, and provides valuable insights. We present the following article in accordance with the MDAR reporting checklist (available at https://dx.doi.org/10.21037/jgo-21-641).

Methods

Tissue samples and cell lines

From Jun. 2017 to Aug. 2019, the Department of Gastrointestinal Surgery, Zhongshan Hospital, Xiamen University collected 162 gastric cancer samples with paired normal tissues. The Zhongshan hospital ethics committee reviewed and approved the experimental protocols (Ethical Approval No. XMZSYYKY-2021-172). All processes were in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from all participants.

Tissues were stored at –80 ℃. GES, MKN28, SGC7901, AGS, MGC803, MKN7, MKN45, BGC823, and HGC27 cells were bought in advance from ATCC (Virginia). Cells

Table 1 sequences of primers for RT-PCR

Names	Sequences (5'-3')
miR-873-5p: Forward	GCAGGAACUUGUGAGUCUCCU
miR-873-5p: Reverse	AGGAGACUCACAAGUUCCUGC
GAPDH: Forward	GTCAGCCGCATCTTCTTT
GAPDH: Reverse	CGCCCAATACGACCAAAT
THUMPD1: forward	AAGGATCAGCAGCCCTCTGGAAGTGAG
THUMPD1: Reverse	CGTTGTCTTCATCAGGACACTTGGGAT

RT-PCR, real-time polymerase chain reaction.

were cultured in RPMI 1640 medium containing 10% Fetal Bovine Serum (FBS, Invitrogen) and incubated at 5% CO_2 and 37 ℃. Six-well plates were used to seed MKN45 cells evenly. DMEM was added overnight with 10% FBS, neither with penicillin nor with streptomycin. As previously described, OPTI-MEM serum-free medium (Sigma Aldrich) as well as Lipofectamine 2000 reagent (Thermo Fisher) were adopted for transfection. In this study, siRNA with 100 nM final concentration was used. Meanwhile, this study also employed the pEZ-Lv201 vector (Biovector) to construct the miR-873-5p overexpression system in AGS cells. The pEZ-Lv201 vector was used as the negative control in normal AGS cells. This study also used lentiviral particles generated with standardized protocols in order to produce plasmids which were highly purified. Endo Fectin-Lenti™ and Titer Boost™ reagents (CWBio) were used to co-transfect AGS cells.

qRT-PCR analysis

Stored at –20 ℃, this study extracted total RNA in each group with M5 SuperTRIgent (mei5bio). As previously described, total RNA was used to synthesize complementary DNA (cDNA) with the iScript supplementary DNA synthesis kit. The PCR reaction system and program were set up as previously described. This study adopted the $2^{-\Delta\Delta Ct}$ cycle method to evaluate the relative expression levels of mRNAs. The relative expression of miR-873-5p, THUMPD1 was normalized to the GAPDH value using $2^{-\Delta\Delta ct}$ values of each sample. All the Forward and Reverse primers are showed in *Table 1*.

Migration and invasion assay

We used the EZCell™ cell Migration/Chemotaxis assay kit (24-well, Biovision, USA) and EZCell™ Cell Invasion Assay (Basement Membrane) (96-well Kit) (Biovision, USA) kits to detect the migration and invasion of MKN45 cells according to the manufacturer's instructions.

CCK8 assay

Cells transfected with the overexpression system and negative control were digested, centrifuged, and resuspended. After that, cells were diluted with complete medium to 2,000 cells/mL. In a 96-well plate, each well was filled with 100 μL of a 2,000 cells/mL suspension. After sticking to the wall, the cell mediums were added Doxorubicin/Fluorouracil and cisplatin according to the gradient concentration, respectively, and then continue to culture for 48 h. In each group, 5 replicate wells were set and were observed them in five-time points. We incubated the plate in an incubator at 37 ℃ for 2 h, and measured the absorbance at OD450. The cell proliferation was subsequently calculated.

Western blot analysis

RIPA Lysis and Extraction Buffer (Beyotime, China) was used to obtain protein from distinct cell groups. Before performing further examination with SDS-PAGE, total protein was reacted with the SDS-PAGE test buffer. Before brooding the layer with anti-Rabbit THUMPD1 (1:2,000) (Abcam, USA) and GAPDH (1:1,000) (CST, USA) for the whole night, we blocked the layer for 1 h. After treating the proteins with the ECL chemiluminescence kit (PromoCell, Germany), and proteins were hatched at room temperature with corresponding secondary antibodies. We observed the bands.

Detection of dual luciferase reporter gene

The cells were co-transfected with THUMPD1 WT/

MUT plasmids or their mutant fragments and miR-873-5p mimic or inhibitor by using lipofectamine 3000 reagent (Invitrogen, USA) according to the protocol. The cells were lysed prior to 36-hour plasmid transfection. We also used the DLR™ Assay System kit (Promega, USA) to directly detect the expression of the luciferase reporter gene, according to the manufacturer's instructions. We used a fluorescent luminometer to measure the firefly luciferase activity. Specifically, we used 50 μL of Renilla luciferase reagent to precisely detect Renilla luciferase activity. The Renilla luciferase fluorescence value and the activity ratio were considered as the internal reference and the reporter gene activity value, respectively.

Statistical analysis

SPSS16.0 statistical software was used for data analysis. The t-test was used for comparisons between the 2 groups, and one-way ANOVA was used for data comparisons between multiple groups. P value <0.05 was considered a significant difference between 2 data points.

Results

MiR-873-5p expression is down-regulated in gastric cancer tissues

We detected the expression of miR-873-5p in gastric cancer tissues and paired normal tissues. The results showed that the expression of miR-873-5p in gastric cancer tissues was significantly lower than that in normal tissues (P<0.001) (*Figure 1A,1B*). To thoroughly probe the biological function of miR-873-5p, we carefully studied miR-873-5p expression in 9 selected cell lines, including GES, MKN28, SGC7901, AGS, MGC803, MKN7, MKN45, BGC823, and HGC27. The qRT-PCR analysis showed that there were significant differences in the expression of miR-873-5p mRNA in these 9 cell lines (*Figure 1C*). It is noteworthy that the expression of miR-873-5p mRNA in AGS cells was significantly lower than that in other cell lines (P<0.001), while the expression of miR-873-5p mRNA in MKN45 cells was significantly higher than that in other cell lines (P<0.001). Therefore, AGS and MKN45 cells were selected for further study. In addition, we investigated the expression of miR-873-5p mRNA in gastric cancer tissues with lymph node metastasis and distant metastasis. The results suggested that miR-873-5p mRNA expression was significantly higher in gastric cancer tissues without distant lymph node metastasis than in gastric cancer tissues with distant lymph node metastasis (P<0.001) (*Figure 1D,1E*). We also tested the relationships between tumor volume and miR-873-5p mRNA expression. *Figure 1F* showed that miR-873-5p mRNA expression was negatively correlated with tumor volume, suggesting that miR-873-5p may be a potential inhibitor of gastric cancer.

Regulation of miR-873-5p in gastric cancer cell migration and invasion

We performed overexpression and knockdown of miR-873-5p in AGS and MKN45 cells. qRT-PCR analysis was further employed to evaluate miR-873-5p expression in AGS and MKN45 cells after different treatments. As shown in *Figure 2A*, miR-873-5p was successfully overexpressed and knocked down in AGS and MKN45 cells. Inhibitor #3 and mimic #3 were used for further study. In addition, the efficiency of miR-873-5p overexpression and knockdown in MKN45 cells and AGS cells were also detected (*Figure 2B*). The results showed that the adopted overexpression and knockdown systems were 2 distinct effective systems.

Moreover, we investigated the regulatory role of miR-873-5p in the migration and invasion of gastric cancer cells in miR-873-5p knockdown treated MKN45 cells and miR-873-5p overexpression treated AGS cells. As shown in *Figure 2C,2D*, miR-873-5p knockdown treatment promoted cell migration and invasion compared with normal MKN45 cells (P<0.01). However, As shown in *Figure 2E,2F*, miR-873-5p overexpression inhibited cell migration and invasion compared with normal AGS cells (P<0.01). Therefore, it is speculated that miR-873-5p mRNA expression is closely related to gastric cancer cell migration as well as cell invasion.

MiR-873-5p inhibits the chemotherapy resistance of gastric cancer cells

Three common chemotherapeutic drugs, cisplatin, doxorubicin, and fluorouracil, were used to study the effect of miR-873-5p expression changes on the chemotherapy sensitivity of gastric cancer cells. We also investigated the proliferation of miR-873-5p knockdown treated MKN45 cells and miR-873-5p overexpression treated AGS cells. As shown in *Figure 3A-3C*, compared with normal AGS cells, the cell survival rate of AGS cells overexpressing miR-873-5p was significantly reduced after treatment with the 3 different drugs (P<0.001). However, compared with normal MKN45 cells, miR-873-5p knockdown MKN45 cells had

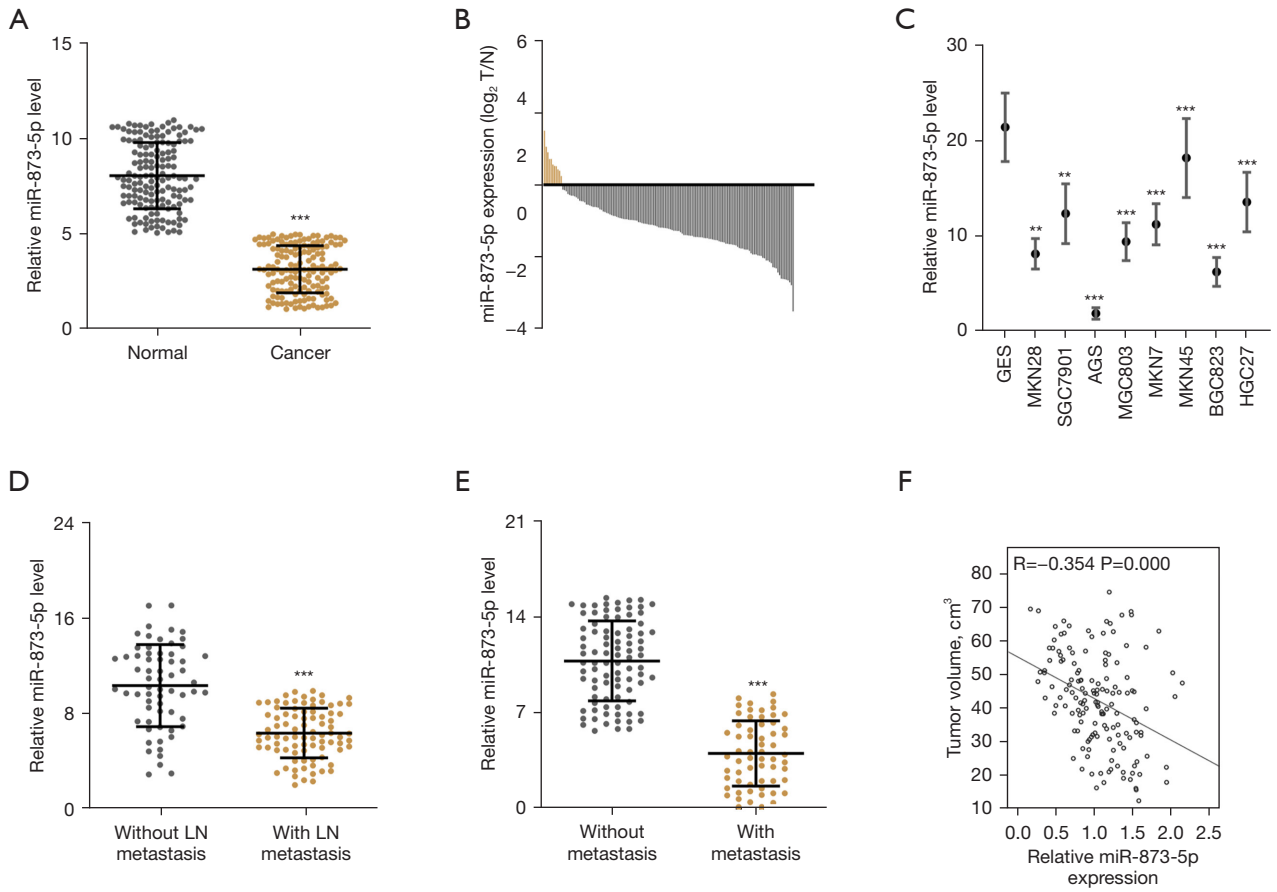

Figure 1 MiR-873-5p expression is down-regulated in gastric cancer. (A) Analysis of the abundance of miR-873-5p in 162 tumor tissues and their paired normal tissues. (B) Analysis of the expression distribution of miR-873-5p in 162 pairs of tumor tissues and adjacent tissues. (C) Abundance analysis of miR-873-5p in 9 cell lines. (D) Abundance analysis of miR-873-5p in tumor tissues with or without lymph node metastasis. MiR-873-5p expression was up-regulated in gastric cancer tissues without lymph node metastasis. (E) Abundance analysis of miR-873-5p in tumor tissues with or without metastasis. MiR-873-5p expression was up-regulated in gastric tumor tissues without metastasis. (F) Relationship analysis between miR-873-5p and tumor volume. **, P<0.01; ***, P<0.001.

significantly increased viability after treatment with all 3 drugs (P<0.001) (*Figure 3D-3F*).

The above evidence shows that miR-873-5p knockdown treatment of MKN45 cells and miR-873-5p overexpression treatment of AGS cells were closely related to changes in cell viability after drug treatment.

MiR-873-5p regulates THUMPD1 protein and mRNA expression

In this study, we screened 2 online databases, DIANA tools and MicroRDB, to acquire the potential targets of miR-873-5p. The results suggested that there were 22 overlapping genes found in the 2 databases. Based on the biological functions, THUMPD1, BSCL2, PTGS1, KRT20, BPGM, TUSC3, PSG11, E2F7, PHF6, DPF2, TNRC6B, and PGM2L1 genes were selected for further analysis (*Figure 4A*). This study also investigated the potential relationship between the abundance of miR-873-5p and the mRNA abundance of THUMPD1, BSCL2, PTGS1, KRT20, BPGM, TUSC3, PSG11, E2F7, PHF6, DPF2, TNRC6B, and PGM2L1 genes in 162 gastric cancer samples (*Figure 4B-4M*).

The results showed that the expression of miR-873-5p was negatively correlated with the mRNA expression of THUMPD1 (P=0.006). Meanwhile, no significant relationships were found between miR-873-5p and BSCL2, PTGS1, KRT20, BPGM, TUSC3, PSG11, E2F7, PHF6,

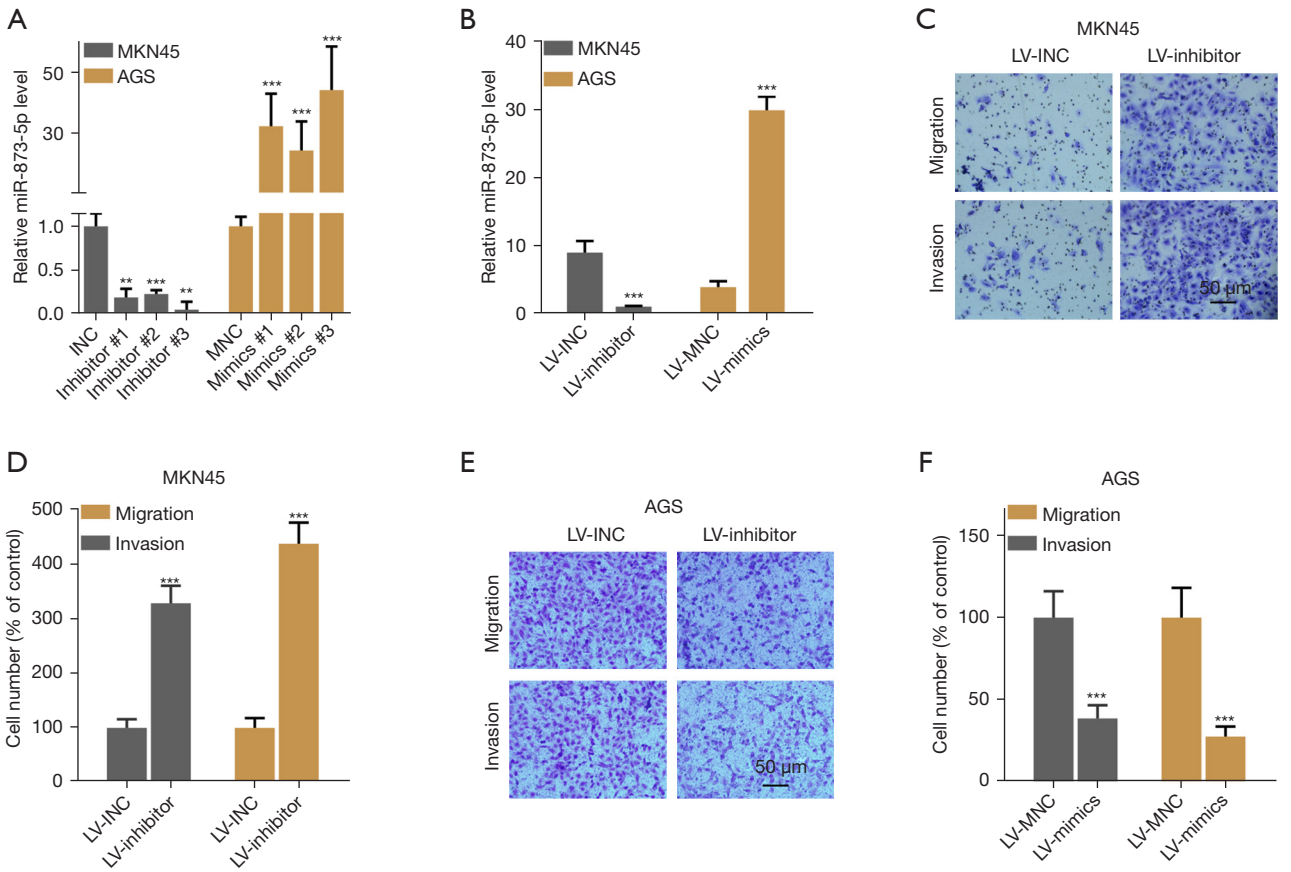

Figure 2 Regulation of miR-873-5p in gastric cancer cell migration and invasion. The invasion and migration of MKN45/AGS cells after treatment with LVs were detected based on the AKP assay. (A) qRT-PCR analysis of miR-873-5p knockdown treated MKN45 cells and miR-873-5p overexpression treated AGS cells. **, P<0.01 means inhibitor# *vs.* inhibitor NC/mimics# *vs.* mimicsNC, ***, P<0.001 means inhibitor# *vs.* inhibitor NC/mimics# *vs.* mimicsNC. (B) Inhibitor 3# in MKN45 cells and mimics 3# in AGS cells were further identified. ***, P<0.001 means LV-inhibitor3 *vs.* LV-inhibitor NC/LV-mimics3 *vs.* LV-mimicsNC. (C,D) Cell migration and invasion analysis of miR-873-5p knockdown treated MKN45 cells. ***, P<0.001 means LV-inhibitor3 *vs.* LV-inhibitor NC. (E,F) Cell migration and invasion analysis of miR-873-5p overexpression treated AGS cells. ***, P<0.001 means LV-mimics3 *vs.* LV-mimicsNC.

DPF2, TNRC6B, and PGM2L1. Therefore, THUMPD1 was solely selected to conduct further study. Moreover, as displayed in *Figure 4N*, the expression of THUMPD1 protein in AGS cells treated with miR-873-5p was significantly lower than that in normal AGS cells (P<0.001). THUMPD1 protein expression was significantly higher in miR-873-5p knockdown MKN45 cells than in normal MKN45 cells (P<0.001).

A similar phenomenon could be found in the qRT-PCR analysis (P<0.001) (*Figure 4N*). The above-mentioned results all suggested that miR-873-5p might affect the THUMPD1 protein as well as mRNA expression.

Furthermore, THUMPD1 mRNA 3'UTR wild type and mutant plasmids for potential binding sites of miR-873-5p were constructed (*Figure 5A*). The DLR™ assay demonstrated that miR-873-5p could not bind to the SGPP1 mutant plasmid, but could bind to the wild type THUMPD1 mRNA 3'UTR (*Figure 5B,5C*). The analysis showed that siRNA 2# was an effective THUMPD1 gene knockdown sequence from the knockdown experiment. Therefore, AGS cells treated with siRNA 2# were selected for further study (*Figure 5D*). In addition, we employed cisplatin, doxorubicin, and fluorouracil to probe the effect of THUMPD1 knockdown on the cell proliferation of miR-873-5p knockdown treated MKN45 cells. As shown in *Figure 5E-5G*, THUMPD1 knockdown significantly

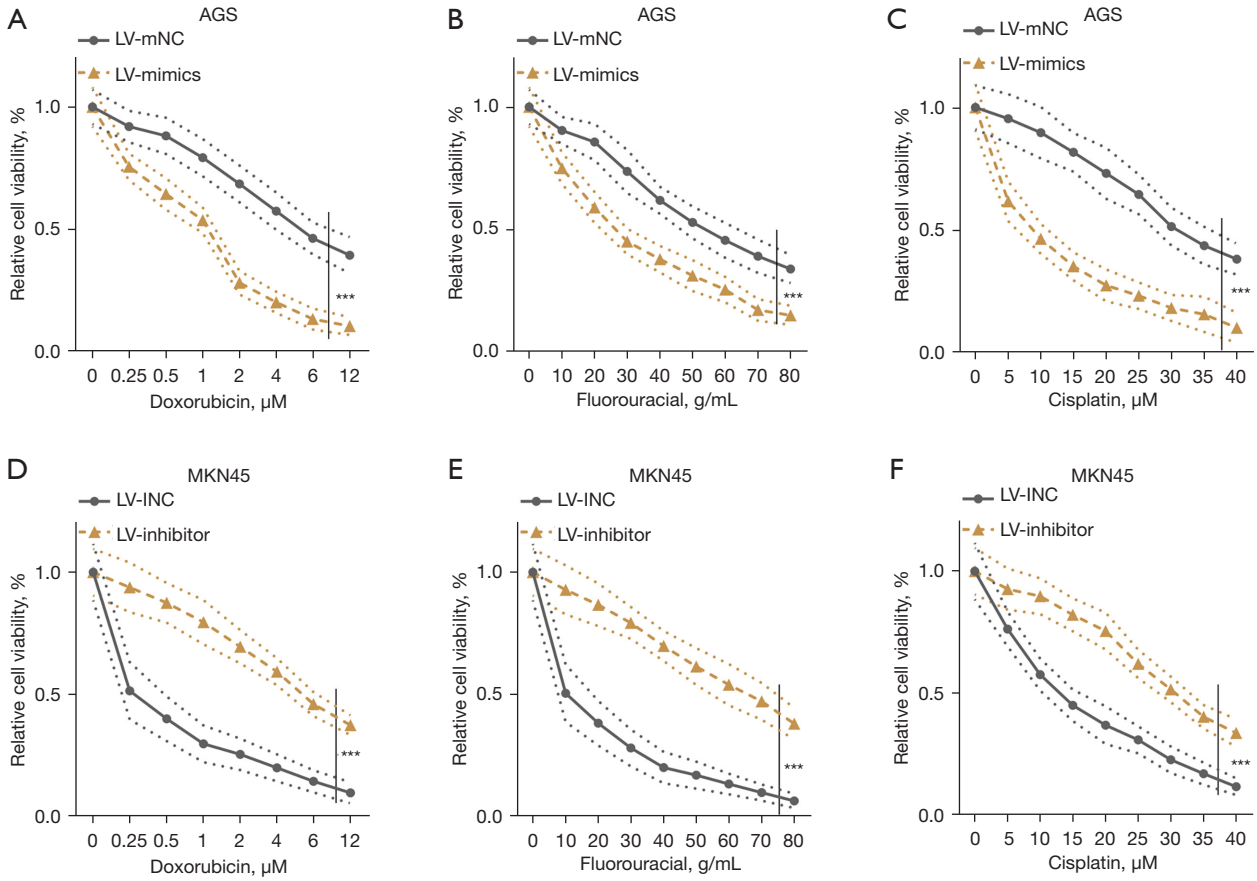

Figure 3 Effect of miR-873-5p on the chemotherapy sensitivity of gastric cancer cells. (A-C) Proliferation analysis of AGS cells overexpressing miR-873-5p after 3 chemotherapeutic drug treatments. (D-F) Proliferation analysis of MKN45 cells with miR-873-5p knockdown after 3 chemotherapy drug treatments. ***, P<0.001.

reduced the cell survival rate in miR-873-5p knockdown MKN45 cells compared with miR-873-5p knockdown MKN45 cells (P<0.001).

Altogether, these results revealed that THUMPD1 knockdown in miR-873-5p knockdown MKN45 cells was closely related to changes in cell viability induced by drug therapy.

Discussion

Exploring and identifying targets for malignant tumor treatment is a crucial topic for cancer research. Gastric cancer, a highly malignant disease with high mortality, has a poor prognosis (22). Currently, although the strategies to prevent gastric cancer are gradually becoming more mature, obstacles and difficulties still exist in the early diagnosis of gastric cancer (23). With the in-depth study of the epidemiology of gastric cancer, it is now widely accepted that the occurrence of gastric cancer appears to be a complex process including multiple factors, multiple genes, and multiple steps (24). Notably, the relationship between miRNAs and gastric cancer has attracted growing attention from researchers in recent years (25). MiRNAs are highly conserved small molecule single-stranded RNAs, which regulate the expression of the target gene by base pairing with the target gene mRNA to guide its degradation or hinder its translation (26). Previous studies have shown that multiple miRNAs are related to gastric cancer, including miR-21, miR-21, miR-29, miR-106, miR-let7a, miR-148, and miR-622, among others. MiR-21, miR-10b, miR-2223, miR-338, miR-let7a, have been confirmed to be tumor markers for evaluating the prognosis of gastric cancer (27). Meanwhile, miR-212 and miR-195 have been proven to be closely related to lymph node metastasis (28). Therefore,

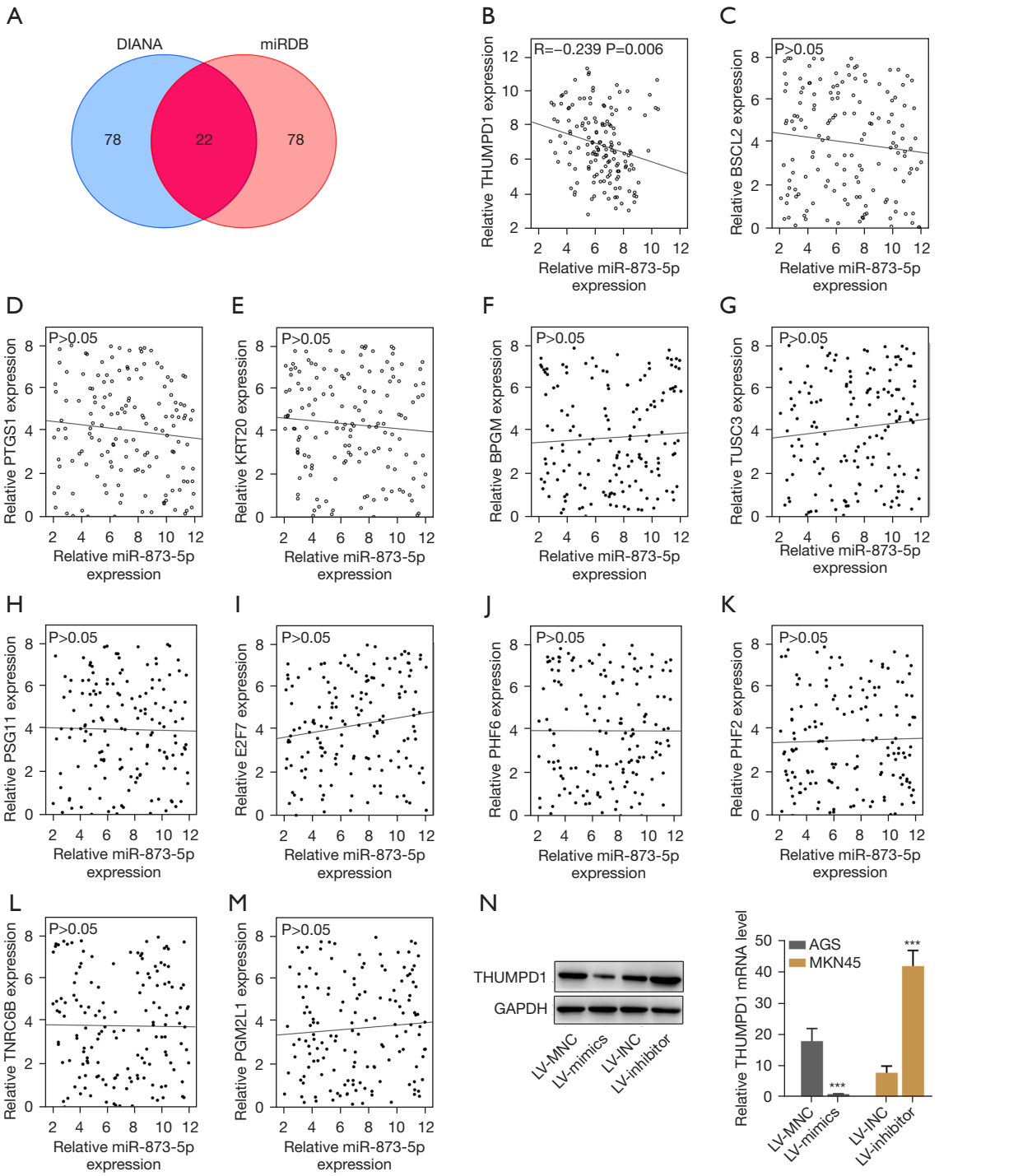

Figure 4 MiR-873-5p plays an important role in gastric cancer through THUMPD1. (A) Venn diagram analysis of potential target genes of miR-873-5p in 2 databases. (B-M) Correlation analysis of miR-873-5p abundance and the mRNA expression of THUMPD1, BSCL2, PTGS1, KRT20, BPGM, TUSC3, PSG11, E2F7, PHF6, DPF2, TNRC6B, and PGM2L1. (N) The qRT-PCR and western blot analysis of THUMPD1 expression in miR-873-5p overexpression treated AGS cells and miR-873-5p knockdown treated MKN45 cells. ***, P<0.001.

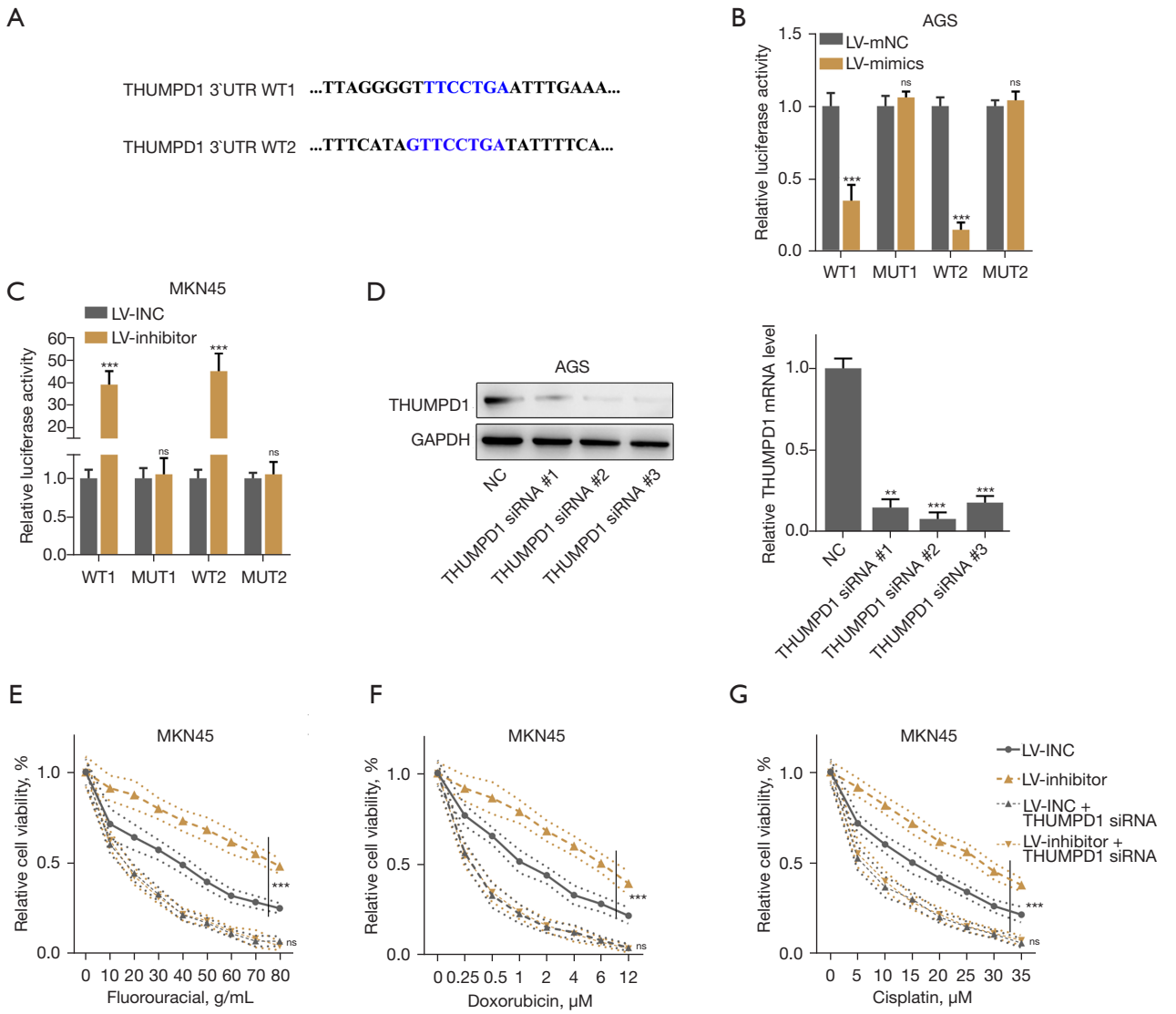

Figure 5 MiR-873-5p directly binds to the 3'UTR of THUMPD1 mRNA. (A) Potential binding sites between miR-873-5p and the 3'UTR of THUMPD1 mRNA. (B,C) Dual luciferase reporter gene analysis of the binding sites between miR-873-5p, wild type, and mutation of the 3'UTR in THUMPD1 mRNA. (D) Protein and mRNA analysis of the THUMPD1 knockdown effect in AGS cells. (E-G) Cell viability analysis after treatment with 3 chemotherapy drugs in miR-873-5p and THUMPD1 knockdown treated MKN45 cells. ***, P<0.001.

novel tumor markers are particularly important for the early diagnosis and individualized treatment of patients.

Previous studies have shown that miR-873-5p is involved in the pathogenesis of a variety of tumors, and is down-regulated in glioblastoma, lung adenocarcinoma, and colorectal cancer (29-31). However, the role of miR-873-5p in gastric cancer remains unknown. The findings of this study suggested that the alteration of miR-873-5p expression might be closely related to the cell proliferation as well as the chemoresistance of gastric cancer. Therefore, miR-873-5p may appear to be a potential target for gastric cancer treatment. Although the hidden mechanism of miR-873-5p in patients with gastric cancer may be complicated and diversified, it still appears to be a molecule that should not be ignored in tumorigenesis and development. This study demonstrated that the expression of miR-873-5p in gastric cancer was lower than that in adjacent tissues. Either the overexpression or knockout of miR-873-5p

could affect the migration, invasion, and chemoresistance of gastric cancer. It is therefore suggested that miR-873-5p dysfunction appears to be an influencing factor for the progression of gastric cancer.

Human THUMPD1 is a specific adaptor protein, which is able to interact with NAT10 for the regulation of tRNA acetylation (18). The study of Havugimana *et al.* demonstrated that THUMPD1 is capable of interacting with Yes-related protein (YAP) (32). YAP plays a role as the main transcriptional co-activator of the Hippo signaling pathway, which is vital in tumor proliferation and tumor invasion (33-34). In addition, a previous study indicated that the invasion and migration of breast cancer cells are promoted by THUMPD1 through the AKT-GSK3β-snail pathway (35). The PI3K/Akt signaling pathway counts as one of the most important signal transduction pathways in cells, which plays a role in the regulation of multiple important biological processes. This signaling pathway has comparatively high status in inhibiting apoptosis as well as promoting proliferation by influencing the activation of downstream effector molecules (36). Studies have also illustrated that the PI3K/Akt signaling pathway could help with tumor invasion as well as metastasis by regulating EMT. For example, Grille *et al.* discovered that the PI3K/Akt signaling pathway participated in the process of induction of EMT in squamous cell carcinoma cells, and could accelerate the invasion and metastasis of tumor cells (37). GSK3β is a multifunctional kinase composed of serine and threonine, which help with regulating glycogen metabolism. It is a downstream gene of the PI3K/Akt signaling pathway and can phosphorylate snail transcription factor to regulate EMT (38). Bai *et al.* suggested that OLA1 regulates EMT through GSK3β/snail/E-cadherin in lung cancer, thus regulating the invasion and metastasis of lung cancer (39). Furthermore, the PI3K/Akt/GSK3β signaling pathway has also been shown to regulate EMT in breast cancer and gastric cancer (35,40). Therefore, as a downstream gene of the PI3K/Akt signaling pathway, GSK3β can phosphorylate snail to regulate EMT and participate in tumor invasion and metastasis. In this study, our results showed that the expression level of THUMPD1 in gastric cancer is closely related to miR-873-5p. Meanwhile, THUMPD1 and miR-873-5p are important in chemotherapy resistance, migration, and invasion. Based on the evidence acquired in this study, we can reasonably speculate that miR-873-5p plays an important role in THUMPD1 regulation, and notably, THUMPD1 seems to be vital in the chemotherapy resistance and functions of gastric cancer cells.

Conclusions

In summary, we demonstrated the expression of miR-873-5p in gastric cancer tissues and cells was downregulated. MiR-873-5p could regulate gastric cancer cell migration, invasion, and chemotherapy resistance through the THUMPD1 axis. Our research first confirmed that miR-873-5p could inhibit gastric cancer cell behavior and chemoresistance by targeting the THUMPD1. The results might help with future studies relevant to gastric cancer by providing detailed information.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The Zhongshan hospital ethics committee reviewed and approved the experimental protocols (Ethical Approval No. XMZSYYKY-2021-172). All processes were in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from all participants.

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