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# MiR-221 affects proliferation and apoptosis of gastric cancer cells through targeting SOCS3

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**Abstract. – OBJECTIVE: The suppressors of cytokine signaling 3 (SOCS3) negatively regulates the JAK-STAT pathway. The bioinformatics analysis revealed a targeted binding site between miR-221 and the 3'-UTR of SOCS3 mRNA. This study investigated the role of miR-221 in the proliferation and apoptosis of gastric cancer cells.**

**PATIENTS AND METHODS: The Dual-Luciferase reporter gene assay validated the target relationship between miR-221 and SOCS3. Gastric cancer tissues were collected and compared with adjacent tissues to detect the expres miR-221 and SOCS3. The Kaplan-Meier was used to analyze the survival rate be n patients with high and low miR-221 expres Human gastric cancer SGC7901 cells were tured and divided into the miR-NC group a miR-221 inhibitor group, follo analysi of the expression of miR-2 SOC p-JAK2 and p-STAT3, cell apoptos nd pro ation.**

**RESULTS: Compared adjac miR-221 expression w s in tumor tissues, an COS expression was decreased. C ared with with lower miR-221 expres he prognos patients with higher mi ession was ificantly worse. The was a ted regulatory relationship b een miR-2 d SOCS3 mRNA. Compar with GES-1 cel iR-221 expression i astric ancer MGC8 3 and SGC7901 was ificant creased, and the expression of 3 m A and rotein was significantly de The t ection of miR-221 inhibitor s cantl creased SOCS3 expression gas SGC7901 cells, decreased p-J 2, p-ST otein expression, increased cell poptosis, a d decreased cell proliferation.**

**CONS: Increased miR-221 expres and eased SOCS3 expression are related to gastric cancer. MiR-221 regulates the iferation and apoptosis of gastric cancer c y regulating SOCS3 expression.**

*Key Words:*
MiR-221, SOCS3, JAK-STAT, Gastric cancer.

## Introducti

Gastric ancer is one of the most common malignant tumo the digestive tract. Its inci ate is the four d the mortality rate i second in common malignant tumors. It has malignanc ast disease progression, low ival rate, an or prognosis[1-3].

tyrosine ase (JAK)-signal transducer and ranscription (STAT) signaling pathway olved in various biological processes, such as cell survival, proliferation, migration, sion[4,5]. The suppressors of cytokine sig- (SOCS3) can directly inhibit the activity of JAK kinase and phosphorylation of its downstream STAT protein, and block the activation and transduction of JAK-STAT signaling pathway[6]. As an important tumor suppressor gene, the abnormal expression or function of SOCS3 plays an important role in the occurrence and progression of various tumors[7-9]. Scholars[10,11] have shown that as a tumor suppressor gene, the abnormal expression or function of SOCS3 is associated with the occurrence, progression, and metastasis of gastric cancer.

MicroRNA is an endogenous non-coding small-molecule single-stranded RNA with approximately 22-25 nucleotides in length in eukaryotes that binds to the 3'-UTR of the target gene mRNA by complementary pairing to degrade or inhibit translation, thus regulating target gene expression. MicroRNA abnormalities are associated with the progression and prognosis of multiple cancers, such as intestinal cancer, kidney cancer, endometrial cancer, ovarian cancer[12-15]. Evidence from studies[16-18] has shown that abnormal expression of miR-221 is closely related to the occurrence, progression, metastasis and prognosis of gastric cancer, suggesting that miR-221 abnormality plays a role in tumor suppres-

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sor or tumor-promoting gene in gastric cancer. The bioinformatics analysis revealed a targeted binding site between miR-221 and the 3'-UTR of SOCS3 mRNA. This study investigated whether miR-221 plays a role in regulating SOCS3 expression, affecting JAK2-STAT3 pathway activity, and gastric cancer cell proliferation and apoptosis.

## Patients and Methods

### Clinical Data

100 patients with gastric cancer who were treated in our hospital from May 2015 to November 2018 were selected, with an average age of 51.9±13.7 years. The tumor tissues removed during the operation and the specimens of the adjacent tissues more than 2 cm away from the tumor tissues were collected, and all the tissue specimens were confirmed by pathological examination. The collections of tissues were informed by the patients and approved the Hospital Ethics Committee.

### Main Reagents and Materials

Human normal gastric mucosal cells GES-1 were purchased from Guangzhou Jini technology (Guangzhou, China), gastric cancer MGC803 and SGC7901 cells were purchased from Beijing Beina Bio (Beijing, China); Roswell Park Memorial Institute 1640 (RPMI-1640) medium was purchased from American Clone (South Logan, UT, USA); [illegible] was purchased from Hangzhou Gini (Hangzhou, China); Fetal bovine serum (FBS) was purchased from Guangzhou Bio (Guangzhou, China); Lipofectamine 2000 and SYBR Green dye were purchased from Invitrogen (Carlsbad, CA, USA); PrimeScript RT reagent was purchased from Dalian TaKaRa (Dalian, China); miR-221 inhibitor, miR-NC, miR-221 mimic were designed and synthesized by Guangzhou Ruibo Bio (Guangzhou, China); Rabbit Anti-human SOCS3 and β-actin antibody were purchased from Santa Cruz Biotechnology (Santa Cruz, CA, USA); rabbit anti-human p-JAK2 and p-STAT3 antibody were purchased from Abcam (Cambridge, MA, USA); Horseradish peroxidase (HRP)-conjugated secondary antibody was purchased from Shanghai Absin (Shanghai, China); pGL3 vector was purchased from Changsha Youbao (Changsha, Chia); the Double-Luciferase activity assay kit was purchased from Promega (Madison, WI, USA); the Annexin V-FITC/PI apoptosis assay reagent was purchased from Togen Chemical (Japan); the EdU-Alexa Fluor 488 cell proliferation assay kit was purchased from Thermo Scientific (Waltham, MA, USA).

### Cell Culture

GES-1, MGC803, and SGC7901 were inoculated in RPMI-1640 medium containing 10% FBS and 1% penicillin, and cultured in a cell incubator containing 5% CO2 at 37°C. After the cells were over, the cells were detected by enzymatic digestion and subcultured at a ratio of 1:5 to 1:6. The experiment was performed when the cells were in logarithmic growth phase.

### Dual-Luciferase Reporter Gene Test

The full-length 3'-UTR fragment of the SOCS3 gene and fragment containing the mutant was amplified using the HEK293T cell genome as a template, and cloned into the pGL3 vector, transformed into DH5α competent cells, and the correct plasmids were sequenced and named as pGL3-SOCS3-WT, pGL3-SOCS3-MUT. pGL3-SOCS3-WT (or pMIR-SOCS3-MUT) and miR-221 inhibitor (or miR-NC) were co-transfected into HEK293T cells with Lipofectamine 2000 reagent. After 48 h of culture, the relative Luciferase activity was measured using Dual-Luciferase reporter assay kit.

### Cell Transfection

SGC7901 cells were cultured *in vitro* and divided into two transfection groups: miR-NC transfection group and miR-221 inhibitor transfection group. The general procedure for transfection was as follows: 10 μL of Lipofectamine 2000, 50 nmoL miR-NC (or miR-221 inhibitor) were diluted with 100 μL of serum-free Opti-MEM, respectively, and incubated for 5 min at room temperature, respectively, and Lipofectamine 2000 and miR-NC (or miR-221 inhibitor), respectively. We gently mixed, incubated for 20 min at room temperature, added the transfectants to the cell culture medium, gently mixed, continued to culture for 72 hours, followed by detection of the related indicators.

### Quantitative Real Time-PCR (qRT-PCR) Detection of Gene Expression

RNA was extracted by TRIzol method, and was reversely transcribed to cDNA using PrimeScriptTM RT reagent Kit, and the resulting cDNA was stored in a refrigerator at -20°C. PCR

amplification was carried out under the action of Taq DNA polymerase using cDNA as a template in a total of 10 μL PCR reaction system including 2×SYBR Green Mixture 5.0 μL, 2.5 μm/L forward primer 0.5 μL, 2.5 μm/L reverse primer 0.5 μL, cDNA 1 μL, ddH2O to make up the volume to 10.0 μL. PCR conditions: 95°C for 5 min, 95°C for 15 s, 60°C for 1 min; fluorescence data was stored on a Bio-Rad CFX96 Real Time-PCR instrument (manufacturer: Bio-Rad; model: CFX96; Hercules, CA, USA) for 40 cycles. The primer sequence for SOCS3-Forward-5′-CCTGCGCCTCAAGACCTTC-3′, SOCS3-Rerverse-5′-GTCACTGCGCTCCAGTAGAA-3′; β-actin-Forward: 5′-GAACCCTAAGGCCAAC-3′, β-actin-Reverse-5′-TGTCACGCACGATTTCC-3′.

### Western Blot

The cells were collected, and the total protein was extracted from the RIPA lysate. After the concentration was determined, 40 μg was applied to the sample, and electrophoresis was carried out for 3 h in the Sodium Dodecyl Sulfate PolyAcrylamide Gel Electrophoresis (SDS-PAGE) gel (12% separation gel, 5% conce[illegible]ed gel), and the protein was electroporat[illegible] mA), transferred to polyvinylidene diflu[illegible]de (PVDF) membrane for 90 min, blocked [illegible] 5% skim milk powder in phosphate-buffe[illegible] saline with Tween® detergent[illegible]T) for 6[illegible] min at room temperature, a[illegible]ed with primary antibody at 4°C [illegible]rnight[illegible]e dilution ratios of SOCS3, [illegible]2, p-[illegible]nd β-actin are 1:2500, 1:[illegible]00[illegible]:80[illegible] spectively), followe[illegible]y was[illegible] times with PBST, and then [illegible]ubated wit[illegible]P-labeled secondary ant[illegible]:5000 dilu[illegible] for 60 min at roo[illegible]empe[illegible]. After washing 3 times with[illegible]BST, the e[illegible]d chemiluminescence (E[illegible]) working solut[illegible]as added to the blotti[illegible]embr[illegible]e and incubated for 1-3 min at r[illegible] temp[illegible]re, followed by exposure and deve[illegible]er[illegible]

### [illegible] Cell Apoptosis

[illegible] above[illegible]oned miR-NC and miR-221 inh[illegible]or transfe[illegible]ion group SGC7901 cells were c[illegible]psinization. After washing twice [illegible]h PBS, [illegible]00 μL of Binding Buffer was added [illegible]the cell pellet and the cells were suspended. 5 [illegible]Annexin V- FITC was added and incubated fo[illegible] minutes in the dark, and then, 5 μL of PI staining was added, followed by analysis of cell apoptosis by flow cytometry.

### EdU Staining for Cell Proliferation

SGC7901 cells were resuspended in RPMI-1640 medium containing 10% FBS, incubated with 10 μM EdU for 120 min, transf[illegible] cells according to the procedure des[illegible]d in [illegible] and cultured for 72 h. After try[illegible] digestion, the cells were collected accordi[illegible]e kit. After centrifugation, washing, fixatio[illegible]meabilization, and incubation of [illegible]reactio[illegible]on the cell proliferation wa[illegible]tected by Be[illegible] Coulter FC 500 MCL [illegible] cytom[illegible] (Brea, [illegible], USA), and the prol[illegible]on a[illegible]y of th[illegible] cells was reflected by t[illegible]pos[illegible] of Ed[illegible]

### Statistical [illegible]ysis

Statistic[illegible] of the data[illegible]s performed using Sta[illegible]ical P[illegible]e for the Social Sciences 18.0 software (SPSS [illegible] Chicago, IL, USA). Th[illegible]rement data w[illegible]xpressed as mean ± s[illegible]ard deviation (SD). The Student's *t*-test was [illegible] to compar[illegible]e measurement data between [illegible]roups. The [illegible]parison of the measurement d[illegible]tween th[illegible]oups was performed by One-way [illegible]variance (ANOVA), and then, by Bon[illegible] method. $p < 0.05$ was considered [illegible]tatistically significant.

## Results

### Abnormal Expression of MiR-221 and SOCS3 in Gastric Cancer

The results of qRT-PCR showed that the expression of miR-221 was significantly increased in tumor tissues of gastric cancer patients compared with adjacent tissues (Figure 1A). The results of qRT-PCR showed that the expression of SOCS3 mRNA in tumor tissues of gastric cancer patients was significantly lower than that of adjacent tissues (Figure 1B).

### Increased Expression of MiR-221 is Associated with Low Survival in Patients with Gastric Cancer

Patients with gastric cancer were divided into miR-221 high expression group and miR-221 low expression group, based on the median miR-221 expression, and the relationship between miR-221 expression and survival rate was analyzed. The analysis showed that the survival rate of patients with higher miR-221 expression was significantly lower than those with lower expression of miR-221 (Log lank test $\chi^2 = 4.582$, $p = 0.032$) (Figure 2).

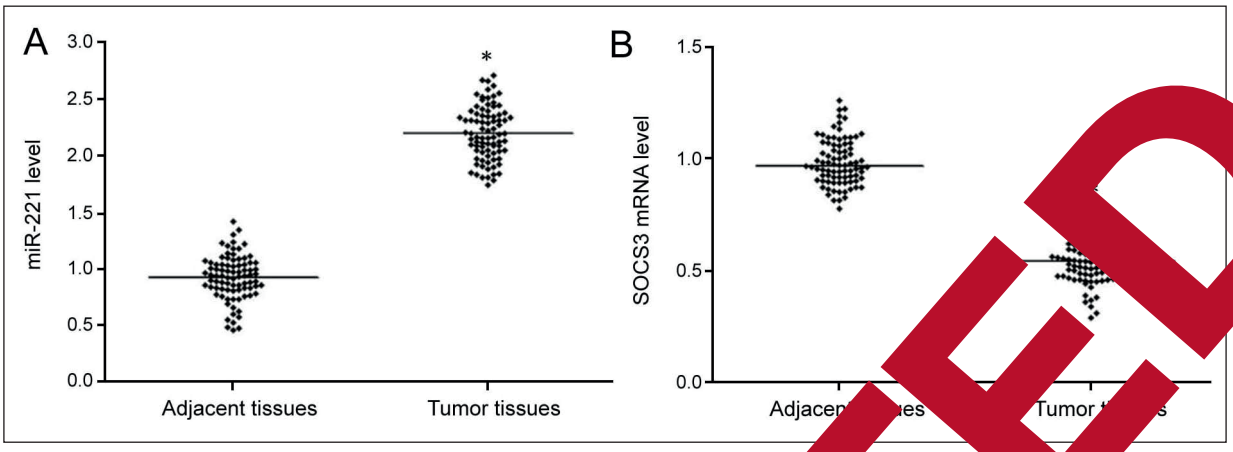


**Figure 1.** Abnormal expression of miR-221 and SOCS3 in tumor tissues of gastric cancer patients. RT-PCR was used to detect the expression of miR-221 in gastric cancer and adjacent tissues. **B,** qRT-PCR was used to detect the expression of SOCS3 mRNA in gastric cancer and paracancerous tissues. *Represents $p < 0.05$ compared with adjacent tissues.



### *A Targeted Relationship Between MiR-221 and SOCS3 mRNA*

The bioinformatics analysis revealed a complementary binding site between miR-221 and the 3'-UTR of SOCS3 mRNA (Figure 3A). The results of the Dual-Luciferase gene reporter assay showed that the transfection of miR-221 mimic significantly reduced the relative Luciferase activity in pGL3-SOCS3-WT transfected HEK293T cells, and the transfection of miR-221 inhibitor significantly increased the relative Luciferase activity in pGL3-SOCS3-WT transfected HEK293T cells, but miR-221 mimic or miR-221 inhibitor had no significant effect on the relative Luciferase activity in pGL3-SOCS3-MUT transfected HEK293T cells (Figure 3B), indicating that miR-221 has a targeted relationship with the 3'-UTR region of SOCS3 mRNA.

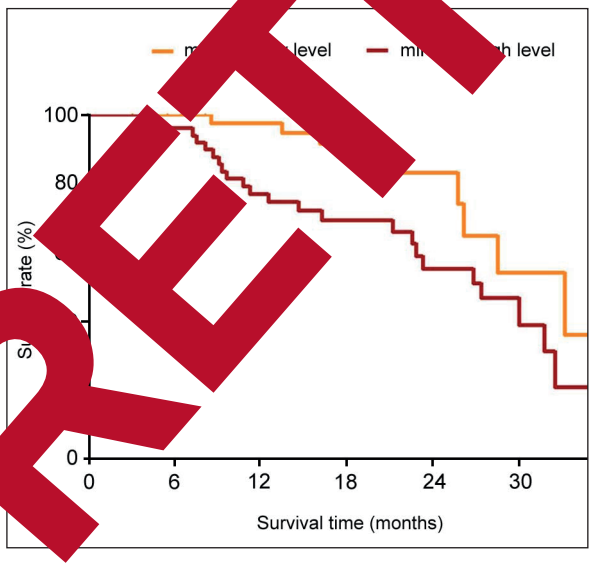


**Figure 2.** Increased expression of miR-221 is associated with low survival in patients with gastric cancer.

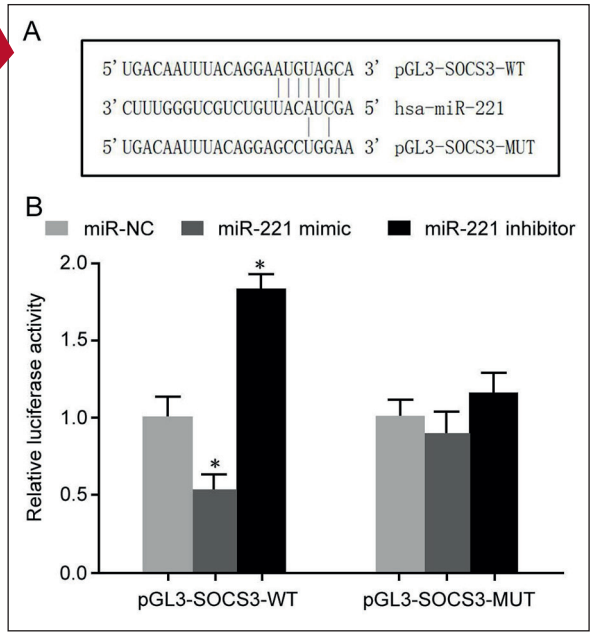


**Figure 3.** There is a targeted regulation relationship between miR-221 and SOCS3 mRNA. **A,** Schematic diagram of the interaction site between miR-221 and the 3'-UTR of SOCS3 mRNA. **B,** Dual-Luciferase gene reporter assay. * represents $p < 0.05$ compared to miR-NC.

### *Abnormal Expression of MiR-221 and SOCS3 in Gastric Cancer Cells*

The results of qRT-PCR showed that, compared with GES-1 cells in normal gastric mucosal epithelial cells, the expression of miR-221 in gastric cancer MGC803 and SGC7901 cells was significantly increased, while the expression of SOCS3 mRNA was significantly decreased (Figure 4A). Western blot analysis showed that the expression of SOCS3 protein in gastric cancer MGC803 and SGC7901 cells was significantly lower than that in normal gastric mucosal epithelial cells (Figure 4B).

### *Downregulation of MiR-221 Expression Can Inhibit Gastric Cancer Cell Proliferation and Promote Apoptosis*

The qRT-PCR results showed that, compared with the miR-NC transfection group, the expression of miR-221 in the SGC7901 cells of the miR-221 inhibitor transfection group was significantly decreased, while the expression level of SOCS3 mRNA was significantly increased (Figure 5A). Western blot analysis showed that, compared with miR-NC transfection group, the expr[illegible] of SOCS3 protein in SGC7901 cells was[illegible] cantly increased in the miR-221 inhibitor [illegible]s-fection group, while the expression of p-J[illegible] and p-STAT3 protein was significantly decrea[illegible] (Figure 5B). Flow cytometry re[illegible]howed th[illegible] the proliferation of SGC790[illegible] signifi-cantly reduced (Figure 5C[illegible]nd cel[illegible]poptosis (Figure 5D) was signifi[illegible]y incr[illegible] the miR-2213 inhibitor tra[illegible]sfe[illegible] with the miR-NC tr[illegible]ection

## Discussion

The pathogenesis of gastric cancer is relatively hidden. Most patients are already in t[illegible] and late stages of cancer. The treat[illegible]is di[illegible] cult, the curative effect is poor, th[illegible]rvival rate is low, and the prognosis is po[illegible]Therefore, detecting pathogenic molec[illegible]les wi[illegible]normal expression during the de[illegible]pment [illegible]tric cancer is of great signif[illegible]ce for explor[illegible] pathogenesis of gastri[illegible]cer, a[illegible]l as for [illegible] proving the therapeu[illegible]fect [illegible]he pro[illegible]nosis.

When a cytoki[illegible]r a[illegible]actor b[illegible] to an intracellular rec[illegible] as a [illegible] the [illegible]ptor can form a hetero[illegible]r and phosp[illegible]e JAK ki-nase. Activ[illegible]an phosphor[illegible] the tyrosine residue o[illegible]AT a[illegible]ivated STAT is separated from the receptor co[illegible] forms a dimer, and is tra[illegible] from the cy[illegible]sm to the nucleus, w[illegible] it acts on specific DNA fragments and reg-[illegible]es gene tran[illegible]ption and expression[4]. SOCS [illegible]negative reg[illegible]r in the JAK-STAT signaling p[illegible]y and pla[illegible] important role in maintaining hom[illegible]cell. As an important tumor sup-pressor g[illegible]e abnormal expression or function of SOCS3 plays an important role in the occurrence [illegible]pression of various tumors, such as breast [illegible] prostate cancer[9], and pancreatic cancer[8]. A number of studies have shown that as a tumor suppressor gene, abnormal expression or function of SOCS3 is associated with the occurrence, progression, and metastasis of gastric cancer[10,11].

Many studies have shown that the expression and function of miR-221 are abnormally changed in various tumors, such as lung cancer[19], breast

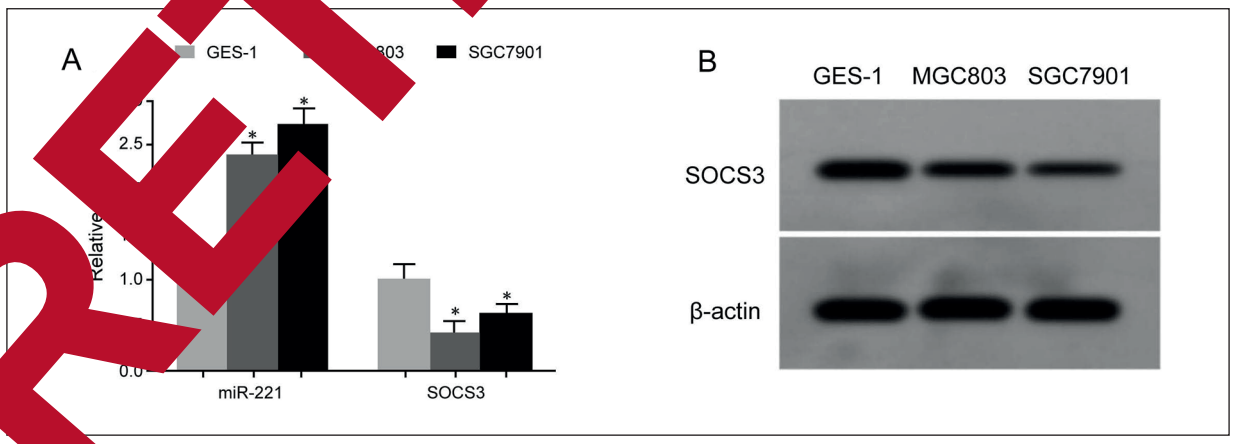


**Figure 4.** Abnormal expression of miR-221 and SOCS3 in gastric cancer cells. **A,** qRT-PCR was used to detect the expression of miR-221 and SOCS3 mRNA in gastric cancer cells. **B,** Western blot was used to detect the expression of SOCS3 protein in gastric cancer cells. *Represents $p < 0.05$ compared to GES-1 cells.

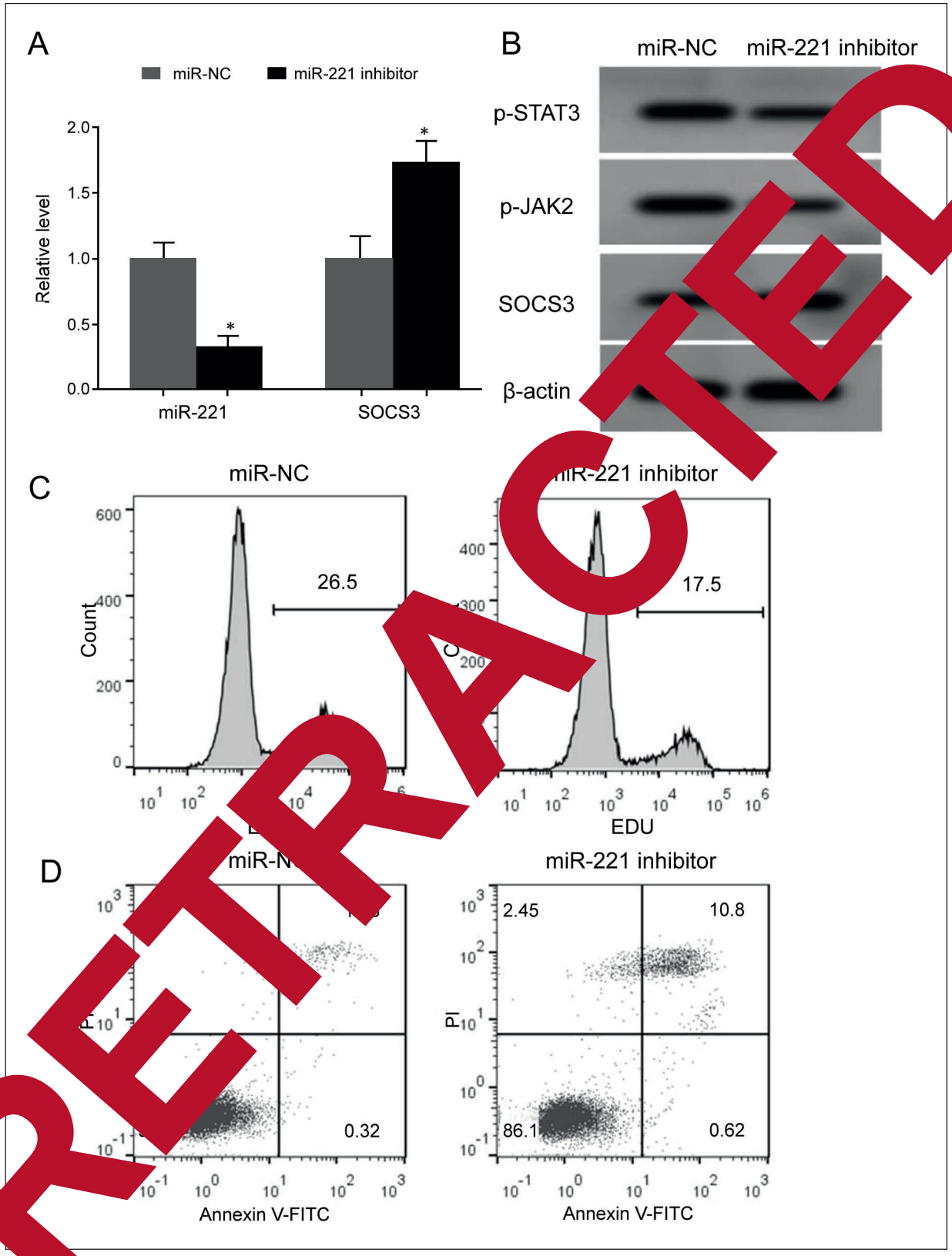




**Figure 5.** Downregulation of miR-221 expression can inhibit gastric cancer cell proliferation and promote apoptosis. **A,** qRT-PCR detection of gene expression. **B,** Western blot detection of protein expression. **C,** Flow detection of cell proliferation. **D,** Flow detection of apoptosis. *Represents $p < 0.05$ compared to miR-NC.

cancer[20], and cervical cancer[21]. Evidence from studies[16-18] has shown that abnormal expression of miR-221 is closely related to the occurrence, progression, metastasis, and prognosis of gastric cancer, suggesting that miR-221 abnormality plays a role in tumor suppressor or tumor-promoting gene in gastric cancer. This study investigated whether miR-221 plays a role in regulating SOCS3 expression, affecting JAK2-STAT3 pathway activity, and the biological effects of gastric cancer cell proliferation and apoptosis.

The results of qRT-PCR showed that compared with the adjacent tissues, the expression of miR-221 was significantly increased in the tumor tissues of gastric cancer patients, while the expression of SOCS3 mRNA was significantly decreased. The survival analysis showed that the survival rate of patients with higher expression of miR-221 was significantly lower than that of patients with lower expression of miR-221, suggesting that the high expression of miR-221 is associated with poor prognosis in patients with gastric cancer. The results of the Dual-Luciferase gene reporter assay showed that the transfection of miR-221 mimic significantly reduced the re[illegible]ve Luciferase activity of pGL3-SOCS3-WT fected HEK293T cells, and that the transf[illegible]n of miR-221 inhibitor significantly increased relative Luciferase activity of pGL3-SOCS3- transfected HEK293T cells an[illegible]firmed th targeted regulation relationshi[illegible]miR-221 and SOCS3 mRNA. In thi[illegible]dy, th[illegible]sults of cell culture *in vitro* sho[illegible]hat co[illegible]with normal gastric epitheli[illegible]G[illegible]e[illegible] sion of miR-221 in[illegible]ric ca[illegible]GC803 and SGC7901 cells w[illegible]nificantly [illegible]sed, while the expression [illegible]3 mRNA wa[illegible]ificantly decreased[illegible]s su[illegible]d that the increased expression[illegible]f miR-221 p[illegible]a role in reducing the exp[illegible]on of SOCS3 [illegible]promoting the patho[illegible]sis of [illegible]astric cancer. In this research mi[illegible]or n[illegible]21 inhibitor was transfected into [illegible]ic [illegible]cer SC[illegible]901 cells *in vitro*, and the bio[illegible]effects[illegible]gastric cancer cells were [illegible]ved t[illegible]sti[illegible]the regulation of miR-221 in [illegible]ric can[illegible]e results of this investigation sho[illegible] that com[illegible]pared with the miR-NC group, th[illegible]of miR-221 inhibitor significantly[illegible]upregulated the expression of SOCS3 mRNA [illegible] protein in SGC7901 cells, decreased the [illegible]sion of p-JAK2 and p-STAT3 protein, inhibi[illegible] cell proliferative capacity, and promoted cell apoptosis, confirming that miR-221 plays a role in promoting cancer by targeting SOCS3 in gastric cancer. In the study of the relationship between miR-221 and gastric cancer, the results of Cai et al[22] showed that the expression of miR-221 in gastric cancer patients was signifi[illegible] creased compared with healthy cont[illegible] and t plasma miR-221 was detected. The [illegible]d under the ROC curve for the differential d[illegible]is of gastric cancer was 0.7960 (95% CI 0.7[illegible]8664). Effatpanah et al[23] showed [illegible]the exp[illegible]of miR-221 was abnormall[illegible]evated in the tissues of gastric canc[illegible]atients[illegible]pared w[illegible] adjacent tissues. The [illegible]unde[illegible]ROC curve of miR-221 for gastri[illegible]an[illegible].9330. [illegible]et al[24] showed that co[illegible]ed wi[illegible]cent[illegible]ues, the expression o[illegible]-221 was ab[illegible]increased in tumor t[illegible]gastric canc[illegible]patients, and the expre[illegible]n of [illegible]21 was increased and related to lymph node [illegible]asis, the clinical stage of [illegible]nd the depth [illegible]umor invasion. The h[illegible]r the expression of miR-221, the lower the [illegible]ival rate and [illegible]e worse prognosis of patients. [illegible]et al[25] found[illegible]t the expression of miR-221 i[illegible]pheral blo[illegible]extracellular bodies of gastric can[illegible]us significantly increased, and the incr[illegible]the miR-221 expression was associated with poor TNM stage and prognosis. The [illegible]of this study showed that the expression [illegible]221 was abnormally elevated in gastric cancer tissues, and that the increase of miR-221 played a role in promoting the genes in gastric cancer, which were consistent with Cai et al[22], Effatpanah et al[23], and Liu et al[24].

Further our investigation showed that transfection of miR-221 inhibitor in gastric cancer SGC7901 cells can significantly increase SOCS3 expression, downregulate the expression of p-JAK2, p-STAT3, inhibit gastric cancer cell proliferation, and promote cell apoptosis, indicating that miR-221 regulates gastric cancer by regulating the SOCS3-JAK/STAT signaling pathway. In the study of the relationship between miR-221 and the biological effects of gastric cancer cells, Liu et al[18] found that *H. pylori* infection can significantly increase the expression of miR-221 and reduce the expression of its target gene RECK, thereby promoting the proliferation and invasion of gastric cancer cells and promoting the onset of gastric cancer. Ma et al[25] showed that exosomes isolated from mesenchymal stem cells transfected with miR-221 mimic can significantly promote the proliferation and migration of gastric cancer BGC-823 and SGC-7901 cells, and enhance the invasion of gastric cancer cells. Ning et al[16] showed that the expression of miR-221 was

abnormally increased in gastric cancer tissues, and the expression of its target gene hepatocyte growth factor activator inhibitor type 1 (HAI-1) was decreased. Moreover, the overexpression of miR-221 in gastric cancer MGC-803 cells can promote the proliferation and migration of gastric cancer cells by inhibiting the expression of HAI-1, while inhibiting the expression of miR-221 can increase the expression of HAI-1, and inhibit proliferation and migration of gastric cancer cells. Wang et al[26] showed that propofol promoted the anti-cancer effect by inhibiting the proliferation of gastric cancer SGC7901, AGS cells, and promoting apoptosis, and the anti-tumor effect of propofol was shown by inhibiting the expression of miR-221. Consistently, the transfection of miR-221 mimic in gastric cancer SGC7901 and AGS cells can antagonize the anti-tumor effect of propofol, confirming the role of miR-221 in the promotion of gastric cancer. The results of this study showed that the downregulation of miR-221 had an anticancer effect of inhibiting gastric cancer cell proliferation and promoting apoptosis, similar to the above findings. This study combines the targeting regulation between mi 21 and SOCS3, revealing that miR-221 play in regulating SOCS3 expression, affecting K-STAT pathway activity, and proliferation apoptosis of gastric cancer cells, which are novelties of our present study. H whet the regulation between miR-2 S3 play an important role *in vivo* is unclea d needs to be confirmed by anim earche limitation of this repo

## usions

The inc sed expres f miR-221 and the decrease OCS3 expressi e related to the patho sis of s tric cancer. iR-221 regulates the ferati nd apoptosis of gastric cancer cell r g SOC xpression.

## Co t of In

The hors declar at they have no conflict of interests.

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