MicroRNA-379 inhibits metastasis and epithelial-mesenchymal transition via targeting FAK/AKT signaling in gastric cancer

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Abstract. Accumulating evidence demonstrates that aberrant miRNAs contribute to gastric cancer (GC) development and progression. However, the roles of various miRNAs in GC remain to be determined. In the present study, we confirmed that a reduced miR-379 expression was present in GC tissues and cell lines. Our clinical analysis revealed that the down-regulated miR-379 expression was significantly correlated with poor prognostic features including lymph node metastasis and advanced TNM stage. Moreover, we confirmed that miR-379 was a novel independent prognostic marker for predicting 5-year survival of GC patients. The ectopic overexpression of miR-379 inhibited cell migration, invasion and EMT progress, while downregulated miR-379 reversed the effect. In addition, miR-379 regulated the focal adhesion kinase (FAK) by directly binding to its 3'-UTR, resulting in suppression of AKT signaling. In clinical samples of GC, miR-379 inversely correlated with FAK, which was upregulated in GC. Alteration of FAK expression or activating AKT signaling at least partially abolished the migration, invasion and EMT progress effects of miR-379 on GC cells. In conclusion, our results indicated that miR-379 functioned as a tumor suppressor gene in regulating the EMT and metastasis of GC via targeting FAK/AKT signaling, and may represent a novel potential therapeutic target and prognostic marker for GC.

Introduction

Gastric cancer (GC) is one of the most common types of cancer worldwide and the second leading cause of cancer-related death globally (1,2). Despite remarkable advance in diagnostic techniques, such as endoscopic detection, and improvement in therapeutic modalities (3), including novel chemotherapeutic interventions and target therapy, the long-term survival of GC patients remains unsatisfactory due to the high rates of local invasion and distal metastasis (4). Therefore, it is critical to identify the potential molecular mechanisms underlying the progression and metastasis in GC and thus, provide novel therapeutic targets for cancer treatment (5).

MicroRNAs (miRNAs) are a group of endogenous and conserved non-coding RNAs that modulate the specific protein expression through binding to the 3'-untranslated region (3'-UTR) of target mRNAs based on sequence complementarity, and function as post-transcriptional regulators of gene expression (6,7). Increasing evidence has confirmed that miRNAs are abnormally expressed in various cancers, including GC (8), and participate in different biological progress including cell growth, apoptosis, differentiation and metastasis (9,10). Therefore, miRNAs have been proposed as promising prognostic markers for GC patients (11).

Among numerous cancer-related miRNAs, miR-379, which is located on chromosome 14q32.31, was recently found to be a novel cancer-related miRNA (12,13). It was downregulated in breast cancer (12,14), glioblastoma (15), hepatocellular carcinoma (16) and malignant pleural mesothelioma (17). miR-379 was decreased in breast cancer and inhibited cell proliferation by regulating cyclin B1 expression (12). miR-379 regulated IL-18 and contributed to drug resistance in malignant pleural mesothelioma (17). miR-379 was decreased in breast cancer and inhibited cell proliferation by regulating cyclin B1 expression (12). miR-379 regulated IL-18 and contributed to drug resistance in malignant pleural mesothelioma (17). miR-379 was found to be upregulated. Elevated miR-379 in prostate cancer facilitated tumor growth, epithelial to mesenchymal transition (EMT) and bone metastasis. Therefore, the functional significance of miR-379 in cancer development and progression seem to be cancer-type specific. However, the expression and functional role of miR-379 in GC have not been elucidated before.

Epithelial-to-mesenchymal transition (EMT) has been recognized as a physiological process in the invasion and metastasis of various cancers through transformation of adherent and polarized epithelial cells into an invasive mesenchymal cell phenotype (19-21). Moreover, cancer cells undergoing the EMT usually decreased the cell adhesion molecule E-cadherin, which is an important determinant of epithelial cell-cell adhesion, while increased the vimentin and N-cadherin expression (22). Accumulating evidence has revealed that EMT can mediate both GC invasion and metas-
teresis (23-25). However, the association between miR-379
and EMT in GC has remained elusive.

In the present study, we investigated the effects of miR-379
on the FAK/AKT signaling in GC cells. Our data showed that
miR-379 was downregulated in the GC and the reduced
miR-379 was associated with poor prognostic features and
poor 5-year survival of GC patients. We also confirmed that
miR-379 could regulate the migration, invasion and EMT
phenotype of GC by targeting FAK/AKT signaling in vitro
and in vivo. These data identify the underlying mechanism
by which miR-379 inhibits migration and invasion of GC and
indicates miR-379 as a novel prognostic biomarker for GC
patients.

Materials and methods

Clinical specimens. Ninety-six GC tissues and paired adjacent
non-cancerous tissues were obtained from the Traditional
Chinese Medicine Hospital of Jingshan County during January
2005 to December 2010. Pathological diagnosis was performed
according to the World Health Organization (WHO) criteria.
None of the patients received chemotherapy or radiotherapy
before surgery. All patients gave written informed consent
and this study was approved by the Ethics Committee of the
Traditional Chinese Medicine Hospital of Jingshan County.

The human GC cell lines SGC7901, MGC803, HGC27,
MKN45 and the normal gastric epithelial cell line GES-1 were
obtained from the Institute of Biochemistry and Cell Biology
of the Chinese Academy of Sciences, Shanghai, China and
were obtained from the Institute of Biochemistry and Cell Biology
MKN45 and the normal gastric epithelial cell line GES-1 were
obtained from the Institute of Biochemistry and Cell Biology
Traditional Chinese Medicine Hospital of Jingshan County.

Western blot analysis. The whole proteins were harvested in
RIPA buffer supplemented with protease and phosphatase
inhibitors (Roche) and the concentrations were quantified with
BCA protein assay kit (Tiangen Biotech, Co., Ltd., Beijing,
China), and an equal amount of 30 µg protein was separated
by 10% SDS-PAGE gel and then transferred onto PVDF
membranes (Millipore, Billerica, MA, USA). The membranes
were blocked with 5% non-fat milk in TBST for 2 h at room
temperature and incubated overnight with specific primary
antibodies (1:1,000; Cell Signaling Technology, Inc., Danvers,
MA, USA) at 4°C. Then the membranes were washed three
times by TBST and incubated with HRP-conjugated
secondary antibody for 2 h at room temperature (SGB-Bio,
Beijing, China). Detection was performed by enhanced chemi-
luminescence kit (Amersham, Little Chalfont, UK). GAPDH
was used as protein loading control. The antibodies against
FAK, E-cadherin, N-cadherin, vimentin, vimentin, and p-AKT
were purchased from Cell Signaling Technology.

Immunohistochemical staining (IHC). Briefly, 4 µm sections
were deparaffinized in xylene, rehydrated through graded
ethanols, followed by blocking of endogenous peroxidase
activity in 3% hydrogen peroxide for 10 min at room tempera-
ture. The corresponding antibody (1:300; Cell Signaling
Technology) was applied as the primary antibody by a strep-
tavidin peroxidase-conjugated (SP-IHC) method. The staining
results were semi-quantitatively evaluated by the multiply of
staining intensity and the percentage of positive staining cells.
The percentage of positive cells was given into four grades:
0 for <5%; 1 for 6-25%; 2 for 26-50%; 3 for 51-75% and 4
for >75%. Staining intensity was assessed by four degrees: 0,
negative; 1, weak; 2, moderate; and 3, strong. Each section was
assayed for ten independent high magnification (x400) fields
to get the average scores.

Cell migration and invasion analyses. Matrigel-uncoated and
-transwell inserts (8 µm pore size; Millipore) were
used to evaluate cell migration and invasion. Briefly, 2x10^4
transfected cells were suspended in 150 µl serum-free RPMI-
1640 medium into the upper chamber, and 700 µl RPMI-1640
medium containing 20% FBS was placed in the lower chamber.
After 24-h incubation, cells were fixed in 4% paraformalde-
hyde for 20 min and stained with 0.1% crystal violet dye for
15 min. The cells on the inner layer were softly removed with a
cotton swab and counted at five randomly selected views, and
the average cell number per view was calculated.

 Luciferase reporter assay. The 3'-UTR sequence of FAK
predicted to interact with miR-379, together with a corre-
sponding mutated sequence within the predicted target sites,
were synthesized and inserted into the pmiR-GLO Dual-lucif-
erase miRNA target expression vector (Promega, Madison,
WI, USA) called wt-FAK 3'-UTR and mt-FAK 3'-UTR.
Subsequently, MGC803 cells that were plated into 24-well
plate and were transfected with miR-379 inhibitor or negative
control. Cells were co-transfected with the wild-type or mutant
3'-UTR of FAK vector using the Lipofectamine 2000 reagent
(Invitrogen). After 48 h, cells were harvested and measured
according to the manufacturer's instructions (Dual-luciferase
assay system; Promega). pRL-TK expressing Renilla luciferase
was cotransfected as an internal control to correct the differ-
ences in both transfection and harvest efficiencies.
Statistical analysis. Data are presented as the mean ± SD and performed at least three independent replicates. SPSS software, 16.0 (SPSS, Inc., Chicago, IL, USA) and Graphpad Prism 6.0 (GraphPad Software, Inc., La Jolla, CA, USA) were used for a two-tailed Student’s t-test, Pearson’s correlation analysis, Kaplan-Meier method and the log-rank test to evaluate the statistical significance. Differences were defined as P<0.05.

Results

The expression of miR-379 is decreased in gastric cancer tissues and cell lines. To investigate whether miR-379 was involved in gastric carcinogenesis, we first examined the expression of miR-379 in 96 pairs of GC tissues and the paired normal gastric mucosa. Our results showed that miR-379 expression in GC tissues was significantly downregulated compared with the paired non-cancerous tissues (P<0.01; Fig. 1A). Moreover, similar result was found in GC cell lines. The data revealed that miR-379 was remarkably reduced in a panel of GC cell lines compared to the normal gastric epithelial cell line (GES-1). n, six repeats with similar results. U6 snRNA was used as internal control. *P<0.05, **P<0.01.

Clinical significance of the downregulated miR-379 expression in GC tissues. To further investigate the role of miR-379 in the progression of GC, we determined the relationship between miR-379 expression and the clinicopathological features and prognosis of GC patients. With the median level of miR-379 as the cut-off, the low miR-379 expression was obviously associated with lymph node metastasis (P<0.001) and advanced TNM stage (P<0.001) (Table I). Moreover, Kaplan-Meier analysis revealed that the downregulation of miR-379 was prominently correlated with shorter overall survival (P=0.0007; Fig. 2A) and shorter progression-free survival (P=0.0002; Fig. 2B).

Table I. The relationship between miR-379 expression and clinicopathological features in GC patients (n=96).

<table>
<thead>
<tr>
<th>Clinical parameters</th>
<th>Cases (n)</th>
<th>miR-379&lt;sup&gt;high&lt;/sup&gt; (n=44)</th>
<th>miR-379&lt;sup&gt;low&lt;/sup&gt; (n=52)</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td>0.986</td>
</tr>
<tr>
<td>&lt;60</td>
<td>35</td>
<td>16</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>61</td>
<td>28</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.439</td>
</tr>
<tr>
<td>Male</td>
<td>66</td>
<td>32</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>30</td>
<td>12</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td></td>
<td></td>
<td></td>
<td>0.156</td>
</tr>
<tr>
<td>&lt;5</td>
<td>72</td>
<td>36</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>24</td>
<td>8</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Histological type</td>
<td></td>
<td></td>
<td></td>
<td>0.238</td>
</tr>
<tr>
<td>Intestinal</td>
<td>78</td>
<td>38</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>18</td>
<td>6</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>TNM stage</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>I+II</td>
<td>40</td>
<td>28</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>III+IV</td>
<td>56</td>
<td>16</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Lymph metastasis</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Present</td>
<td>58</td>
<td>18</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>38</td>
<td>26</td>
<td>12</td>
<td></td>
</tr>
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</table>

<sup>a</sup>P<0.05 statistically significant.

Figure 1. Expression of miR-379 in GC tissues and cell lines. (A) Quantification of the data revealed that the mean level of miR-379 expression in GC tissues was significantly lower than that in matched adjacent non-cancer tissues. (B) Comparing differences in the expression levels of miR-379 between GC cell lines compared to the normal gastric epithelial cell line (GES-1). n, six repeats with similar results. U6 snRNA was used as internal control. *P<0.05, **P<0.01.

Figure 2. The prognostic value of miR-379 for GC patients. GC patients with lower expression of miR-379 had worse (A) overall survival and (B) progression-free survival. **P<0.01.
Furthermore, miR-379 expression was an independent factor for predicting both 5-year overall and progression-free survival in GC patients (P=0.012, P=0.014, respectively; Table II). These results indicate that miR-379 may act as a potent biomarker for predicting prognosis of GC patients.

Table II. Multivariate Cox regression analysis of 5-year OS and PFS of 96 GC patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall survival</th>
<th>Progression-free survival</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>miR-379 expression</td>
<td>0.212</td>
<td>0.056-0.892</td>
</tr>
<tr>
<td>TNM stage</td>
<td>2.563</td>
<td>1.317-5.982</td>
</tr>
<tr>
<td>Lymph metastasis</td>
<td>3.243</td>
<td>1.572-6.238</td>
</tr>
</tbody>
</table>

HR, hazard ratio; CI, confidence interval; \(a\)Statistically significant.

in GC patients. Furthermore, miR-379 expression was an independent factor for predicting both 5-year overall and progression-free survival in GC patients (P=0.012, P=0.014, respectively; Table II). These results indicate that miR-379 may act as a potent biomarker for predicting prognosis of GC patients.

miR-379 inhibits GC cell migration and invasion. To explore the biological function of miR-379 in HCC, we transduced GC cell lines with miR-379 expression vector or anti-miR-379 vector which contained different endogenous miR-379 levels. As determined by qRT-PCR, we confirmed that miR-379 effectively upregulated miR-379 in MGC803 cells (P<0.05; Fig. 3A) or downregulated miR-379 in SGC7901 cells (P<0.05; Fig. 3C). As examined by Matrigel-coated (for invasion) and -uncoated (for migration) Transwell assays, miR-379 overexpression significantly inhibited the migration and invasion of MGC803 cells (P<0.05; Fig. 3B), whereas
miR-379 knockdown obviously increased the number of migrated and invaded SGC7901 cells (P<0.05; Fig. 3D). In conclusion, these data suggested that miR-379 could regulate the GC cell migration and invasion and may exert an anti-metastatic effect on GC.

miR-379 suppresses epithelial-to-mesenchymal transition in GC cells. EMT has been proposed as a critical role in the initiation of metastasis progression of cancer. To gain a mechanistic illustration of the potential role of miR-379 in modulating GC metastasis, the EMT markers were measured. We found that miR-379 overexpression facilitated the epithelial marker E-cadherin and suppressed N-cadherin and vimentin expression (P<0.05; Fig. 4A). In contrast, miR-379 knockdown decreased E-cadherin expression and increased N-cadherin and vimentin expression (P<0.05; Fig. 4B). In addition, we further explored the correlation between miR-379 expression and EMT marker in GC tissues. We found that the E-cadherin expression in high miR-379 group was higher than that in low miR-379 group. Conversely, the expression level of vimentin in the high miR-379 group was markedly lower than that in low miR-379 group (P<0.05; Fig. 4C). Taken together, these results suggest that miR-379 function as a suppressor of EMT in GC cells.

FAK is a direct downstream target of miR-379 in GC cells. To elucidate the molecular mechanisms responsible for the functional influence of miR-379 in GC cells, we searched the publically available database TargetScan to explore the candidate target genes. Among them, FAK was known to play an important role in GC invasion and metastasis (26). As shown in Fig. 5A, the sequence complementary to the binding sites of miR-379 was revealed in the 3'-UTR of FAK. We performed a luciferase reporter assay to verify that miR-379 could bind to the 3'-UTR of FAK. The results showed that miR-379 overexpression significantly decreased the luciferase activity of wild-type (wt) FAK 3'-UTR while had no influence on that of mutant (mt) FAK 3'-UTR (P<0.05; Fig. 5B). On the contrary, miR-379 knockdown increased the luciferase activity of wt FAK 3'-UTR (P<0.05; Fig. 5B) but did not affect the luciferase activity of mt FAK 3'-UTR constructs. In addition, miR-379 overexpression markedly reduced the mRNA and protein levels of FAK in MGC803 cells (P<0.05, respectively; Fig. 5C and D). By contrast, the
expression of FAK mRNA and protein were significantly increased by the downregulation of miR-379 in SGC7901 cells (P<0.05, respectively; Fig. 5C and D).

**miR-379 correlates negatively with the FAK expression in GC samples.** To further evaluate the relationship between miR-379 and FAK in GC tissues, we measured the FAK mRNA and
protein expression in two groups of miR-379. As expected, our data showed that both FAK mRNA and protein expression level in high miR-379 group were significantly lower than that in low miR-379 group in GC (P<0.05; Fig. 6A and B). Moreover, we demonstrated that the mRNA level of FAK in the GC tissues was inversely correlated with miR-379 expression (R²=0.6737, P<0.0001; Fig. 6C). Consistently, as assessed by IHC assay, FAK protein expression in miR-379 high-expressing tumors was obviously lower than miR-379 low-expressing tumors (P<0.05; Fig. 6D), which was similar with previous studies. In conclusion, these data suggest that FAK was a direct downstream target of miR-379 in GC.

**Figure 7.** Alterations of FAK partially abolish miR-379-mediated GC cell migration, invasion and EMT progress. (A) miR-379-overexpressing MGC803 cells that were transfected with EV or FAK expression plasmid were subjected to western blot analysis for FAK. (B) Cell migration and invasion of the miR-379-overexpressing MGC803 cells was increased by FAK overexpression. (C) miR-379-suppressive SGC7901 cells that were transfected with scrambled siRNA or FAK siRNA were subjected to western blot analysis for FAK. (D) FAK knockdown abrogated the effects of miR-379 knockdown on SGC7901 cells. (E) Western blot analysis of EMT marker proteins in MGC803 cells stably expressing miR-379 transduced with FAK or control vector. (F) Western blot analysis of indicated proteins in SGC7901 cells stably expressing miR-379 inhibitor transfected with FAK siRNA or control siRNA. n, six independent experiments. EV, empty vector. *P<0.05.

**FAK is essential for the miR-379-mediated inhibition of cell migration, invasion and EMT in HCC cells.** To clarify that FAK is a functional target of miR-379, FAK was overexpressed by a plasmid vector in miR-379-overexpressing MGC803 cells (P<0.05; Fig. 7A). Furthermore, FAK overexpression increased cell migration, and invasion (P<0.05, respectively; Fig. 7B) and promoted EMT progress (P<0.05; Fig. 7E). Similarly, FAK knockdown by a specific siRNA in miR-379-suppressive SGC7901 cells (P<0.05; Fig. 7C) significantly inhibited cell migration, invasion (P<0.05, respectively; Fig. 7D) and EMT progress (P<0.05; Fig. 7F). These data demonstrated that FAK is a downstream mediator in the function of miR-379 in GC.
PI3K/AKT signaling is essential for the biological function of miR-379 in GC. Previous studies demonstrated that FAK could induce the activation of PI3K/AKT signaling and play a critical role in the invasion and metastasis of GC and EMT (27,28). As shown in Fig. 8A, ectopic expression of miR-379 significantly decreased, while miR-379 knockdown increased the AKT phosphorylation in GC cells (P<0.05; Fig. 8A). However, the total AKT protein had no change (P<0.05; Fig. 8A). These data indicate that miR-379 suppressed the PI3K/AKT pathway in GC cells. To determine whether AKT phosphorylation mediated miR-379-induced inhibition of cell migration, invasion and EMT process in GC cells, we treated miR-379-overexpressing MGC803 cells with insulin-like growth factor 1 (IGF-1), which is an activator of PI3K/AKT pathway. We found that IGF-1 at least partially rescued the miR-379-induced inhibition of cell migration, invasion (P<0.05; Fig. 8B) and EMT process (P<0.05; Fig. 8D). Conversely, the restraint of the PI3K/AKT pathway by MK2206 abrogated the effects of miR-379 inhibition to induce cell migration, invasion (P<0.05; Fig. 8C) and EMT progress (P<0.05; Fig. 8D) in miR-379-suppressive SGC7901 cells. Taken together, our results demonstrate that PI3K/AKT signaling plays an essential function during miR-379-induced GC cell migration, invasion and EMT progression.

Discussion

Systemic metastasis of GC is the major cause of the tumor recurrence and patient mortality. Increasing evidence has demonstrated that miRNAs were involved in GC invasion and metastasis (29,30). Therefore, miRNAs have been regarded as potential biomarkers and therapeutic targets for GC. In previous studies, Chen et al (16) demonstrated that microRNA-379-5p inhibited tumor invasion and metastasis by targeting FAK/AKT signaling in hepatocellular carcinoma (HCC), moreover, miR-379 suppressed HCC metastasis and EMT in vivo. In addition, Khan et al (12) confirmed that miR-379 was decreased in breast cancer and could be a novel
regulator of cyclin B1. However, on the contrary, miR-379 in the DLK1-DIO3 miRNA mega-cluster regulated EMT and bone metastasis of prostate cancer (13). Moreover, miR-379 was downregulated in papillary renal cell carcinoma and significantly associated with patient survival (18). These data indicated that the expression level and biological effect was dependent on the cancer type.

In the present study, we found that miR-379 was significantly downregulated in 96 GC tissues compared with the corresponding non-cancerous tissues. Similarly, the expression level of miR-379 in gastric cancer cell lines were significantly decreased. Reduced miR-379 expression was obviously correlated with malignant clinicopathological characteristics of GC patients, including advanced TNM stage and lymph node metastasis. Moreover, we found that low miR-379 group had a significantly worse 5-year OS and PFS for GC patients. Multivariate Cox regression analysis indicated that miR-379 was an independent prognostic factor for predicting survival of GC patients. Taken together, these results suggest that miR-379 is critical for prognosis outcome of GC patients. Importantly, gain- and loss-function experiment demonstrated that miR-379 inhibited cell migration, invasion and EMT, at least partially by targeting FAK mediated PI3K/AKT signaling pathway. Furthermore, miR-379 was inversely correlated with FAK expression, which was elevated in GC tissues (31). In addition, miR-379 could negatively modulate FAK accumulation in GC cells. Taken together, these results demonstrated that miR-379 functions as a tumor suppressor in the migration, invasion and EMT of GC by directly inhibiting FAK/AKT pathway.

FAK, a non-receptor tyrosine kinase, plays a critical role in integrin signaling and promotes cancer progression, invasion and metastasis (32). Increased FAK expression was positively associated with poor survival and cancer progression in different cancers, including GC (33). FAK/PI3K/AKT signaling was found to promote EMT progression, which was proposed as a vital mechanism that regulates the initial steps of
metastatic progression of cancer (34). Our results showed that AKT pathway abolished the inhibitory or stimulatory effect of miR-379 on GC cells. Taken together, these data demonstrated the suppressive effect of miR-379 was mediated by targeting FAK to inhibit AKT phosphorylation pathway in GC.

In summary, we demonstrated that miR-379 was downregulated in GC tissues and cell lines, and its decreased expression was correlated with malignant clinicopathological features. Furthermore, we confirmed that miR-379 inhibited cell migration, invasion and EMT by inhibiting FAK-mediated PI3K/AKT signaling pathway. These results suggest that miR-379 is a potential metastasis-associated tumor suppressor in GC. Collectively, the deregulation of miR-379 may play an important role in tumor metastasis and may be a novel prognostic factor and potential therapeutic target for GC.

References