MicroRNA-383-5p predicts favorable prognosis and inhibits the progression of diffuse large B-cell lymphoma

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Abstract. The roles of microRNA (miRNA/miR)-383-5p have been reported in several malignancies, including breast cancer, gastric cancer, ovarian cancer and lung adenocarcinoma. However, its function in diffuse large B-cell lymphoma (DLBCL) remains unclear. Thus, the present study aimed to investigate the role of miR-383-5p in DLCBL. Reverse transcription-quantitative PCR analysis was performed to detect miR-383-5p expression in 80 paired tissue samples from patients with DLBCL and control subjects, as well as related cancer cell lines. Kaplan-Meier survival analysis was performed, and the prognostic value of miR-383-5p was determined via Cox regression analysis. Furthermore, the association between miR-383-5p expression and the clinicopathological characteristics of patients with DLBCL was investigated. The Cell Counting Kit-8, crystal violet staining and Transwell assays were performed to assess the effects of miR-383-5p on cell proliferation and invasion, respectively. The results demonstrated that miR-383-5p expression was upregulated in human DLBCL tissues and cell lines. In addition, miR-383-5p expression was closely associated with clinical stage and extranodal invasion in patients with DLBCL. Notably, high miR-383-5p expression was able to predict a favorable clinical prognosis in patients with DLBCL. Furthermore, overexpression of miR-383-5p significantly inhibited the proliferation and invasion of DLBCL cells, the effects of which were reversed following miR-383-5p knockdown. Taken together, the results of the present study suggest that miR-383-5p may predict favorable prognosis, and thus may be used as a prognostic biomarker for patients with DLBCL. In addition, miR-383-5p appears to play critical roles in inhibiting the proliferation and invasion of DLBCL cells, and thus may be used as a potential therapeutic target in patients with DLBCL.

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Introduction

Lymphoma is one of the most common cancers worldwide, with an incidence approximately 6.68 per 100,000 people, and develops in hematological and lymphoid compartments, including lymph nodes, spleen and thymus, as well as extranodal lymphatic tissues and organs (1,2). Diffuse large B-cell lymphoma (DLBCL) accounts for ~30.0% of non-Hodgkin's lymphoma in western countries and 45.8% in China (3). The incidence of DLBCL continues to increase (4,5). Notably, DLBCL is a clinically, pathologically and molecularly heterogeneous entity, with a 5-year survival rate of 32-81% (6). Despite improvements in its response rate to rituximab, and combination with chemotherapy and other novel treatment modalities, such as promising immunotherapy, a significant proportion of patients with DLBCL exhibit strong refractory and relapse trends, thus the long-term prognosis of this disease remains unsatisfactory (7). Thus, identification of novel prognostic biomarkers and therapeutic targets for effective diagnosis and treatment of patients with DLBCL is of great importance.

MicroRNAs (miRNAs/miRs) are small non-coding RNAs, 20-25 nucleotides in length (8). Recently, several studies have demonstrated that miRNAs are involved in an extensive range of biological processes, including cell proliferation, migration, invasion, and apoptosis (9-11). In addition, some miRNAs act as oncogenes or tumor suppressor genes in different types of cancer (12-14). miR-383-5p is located at chromosome 8p22 in humans (15), and its role as a tumor suppressor has been investigated in several malignancies, including breast (15), gastric (16,17) and ovarian cancers (18), as well as lung adenocarcinoma (19) and oral squamous cell carcinoma (20). With regards to DLBCL, several studies have reported that some miRNA signatures are closely associated with characteristics of patients with DLBCL, including cell proliferation, migration, invasion and chemotherapy-resistance, as well as clinical practice (21-23). However, the biological function and prognostic value of miR-383-5p in DLBCL remains unclear.

The present study aimed to investigate the biological functions and determine the prognostic value of miR-383-5p in DLBCL progression. The expression pattern of miR-383-5p, as well as its association with clinicopathological characteristics of patients with DLBCL were assessed. The *in vitro* effects of miR-383-5p on the proliferation and invasion of DLBCL cells was also investigated.

Materials and methods

Patient samples and clinical follow-up. A total of 80 patients with DLBCL at the Second Affiliated Hospital of Harbin Medical University (Harbin, China) were enrolled in the present study between January 2012 and December 2016. The inclusion criteria were as follows: Patients with DLBCL underwent routine R-CHOP and received no previous chemotherapy or radiation. Patients with incomplete follow-up data, including clinicopathological characteristics and survival time were excluded from the present study.

DLBCL tissue samples were collected via biopsy and stored at -80˚C until subsequent experimentation. Control biopsy tissue samples (n=80) were collected from patients with reactive lymphoid hyperplasia (RLH, suspected of lymphoma). The pathological status of all samples was independently confirmed by two pathologists at the Second Affiliated Hospital of Harbin Medical University. Patients with DLBCL were assessed once every 4-6 months, until death or dropout from the telephone follow-up program. The follow-up program was between January 2012 and December 2019. Clinical parameters and survival information were recorded accordingly. The clinical parameters included age, sex, B symptoms, clinical stage (24), extranodal invasion, serum lactate dehydrogenase (LDH) levels and International Prognostic Index (IPI) score (25). Patient follow-up was censored on December 2019. The present study was approved by the Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (Harbin, China; approval no. ASHHM000152), and performed in accordance with the Declaration of Helsinki. Written informed consent was provided by all patients prior to the study start.

Classification of patients. Patients were divided into two groups (miR-383-5p low and high expression groups), based on median miR-383-5p expression or the 25th percentile miR-383-5p expression. Overall survival (OS) was defined from the time of treatment to death or last follow-up, while disease-free survival (DFS) was defined from the time of treatment to recurrence, death or last follow-up.

Reverse transcription-quantitative (RT-q)PCR. Total miRNA was extracted from fresh tissues using the RNA Extraction kit (Qiagen, Inc.), according to the manufacturer's protocol, and reverse transcribed into cDNA using the RT kit (Shanghai GenePharma Co., Ltd.). The temperature protocol for RT was 51˚C for 20 min, followed by 82˚C for 10 min. A miR-383-5p-specific primer and probe (TaqMan MicroRNA Assay kit, Applied Biosystems; Thermo Fisher Scientific, Inc.) were used to detect expression levels, using an ABI 7500 FAST Real-Time PCR system (Applied Biosystems; Thermo Fisher Scientific, Inc.). The following thermocycling conditions were used for qPCR: Initial denaturation at 94˚C for 2 min, followed by 40 cycles of 94˚C for 10 sec, 55˚C for 30 sec and 72˚C for 20 sec. The following primer sequences were used for qPCR: miR-383-5p forward, 5'-GGGAGATCAGAAGGTGATTGTGGCT-3' and reverse, 5'-CAGTGCGTGTCGTGGAGT-3'; and U6 forward, 5'-CTCGCTTCGGCAGCACA-3' and reverse, 5'-AACGCTTCACGAATTTGCGT-3'. Relative miR-383-5p expression levels were calculated using the $2^{-\Delta\Delta Cq}$ method (26) and normalized to the internal reference gene U6.

Cell culture and transfection. Human DLBCL cell lines, OCI-LY7 and OCI-LY3, and normal B lymphocytes, IM-9I, were purchased from the American Type Culture Collection. OCI-LY7 and OCI-LY3 cells were maintained in IMEM medium (Gibco; Thermo Fisher Scientific, Inc.) supplemented with 10% fetal bovine serum (FBS; Thermo Fisher Scientific, Inc.), while IM-9I cells were maintained in RPMI-1640 culture medium (Gibco; Thermo Fisher Scientific, Inc.) supplemented with 10% FBS. All cells were cultured at 37˚C with 5% CO_2.

miR-383-5p mimic, miR-383-5p inhibitor and corresponding negative controls (NC) were purchased from Shanghai GenePharma Co., Ltd.. Once they reached 70% confluence, $2x10^5$ cells were transfected with 50 nM miR-383-5p mimic, miR-383-5p inhibitor and/or respective controls, using Lipofectamine® 2000 reagent (Invitrogen; Thermo Fisher Scientific, Inc.) at 37˚C for 3 h, according to the manufacturer's protocol. The following sequences were used: miR-383-5p mimic, 5'-AAAUCUCUGCAGGCAAAUGUGA-3' and mimic-NC, 5'-UUCUCCGAACGUGUCACGUTT-3'; and miR-383-5p inhibitor, 5'-CAGUGGUUUUACCCUAUGGUAG-3' and inhibitor-NC, 5'-UUCUCCGAACGUGUCACGUTT-3'. Cells were harvested for subsequent experimentation 48 h post-transfection.

Cell counting kit-8 (CCK-8) assay. Transfected cells were seeded into 96-well plates at a density of $1x10^4$ cells/well. CCK-8 reagent (10 μl, Dojindo Molecular Technologies, Inc.) was added to each well at 0, 24, 48, and 72 h, and incubated at 37˚C for an additional 2 h. Cell proliferation was subsequently analyzed at a wavelength of 450 nm, using an automatic microplate reader (BioTek Instruments).

Crystal violet staining. Crystal violet staining was performed to assess cell proliferation. Transfected cells were seeded into 6-well plates at the density of 1,000 cells/well and cultured in IMEM medium (Gibco; Thermo Fisher Scientific, Inc.) supplemented with 10% FBS at 37˚C. Culture medium was replaced every 3 days for a total of 2 weeks. Cells were subsequently fixed with 100% methanol for 5 min at room temperature and stained with 0.5% crystal violet solution for 10 min at room temperature. Cells were washed three times with PBS and observed under a light microscope (magnification, x4). Cell proliferation was subsequently analyzed at a wavelength of 570 nm, using an automatic microplate reader.

Transwell assay. The Transwell assay was performed to assess cell invasion. A total of 100 μl cell suspension without FBS ($4x10^4$ cells) was plated in the upper chambers of 24-well Transwell plates (Corning, Inc.), with 8 μm pore size membranes. IMEM medium (Gibco; Thermo Fisher Scientific, Inc.) (500 μl) supplemented with 10% FBS was plated in the lower chambers. Membranes were pre-coated with 50 μl Matrigel (BD Biosciences) for 4 h at 37˚C. Following incubation for 24 h at 37˚C with 5% CO_2, the invasive cells were fixed with 100% methanol for 5 min at room temperature and stained with 0.1% crystal violet for 10 min at room temperature. Stained cells were counted in five randomly selected

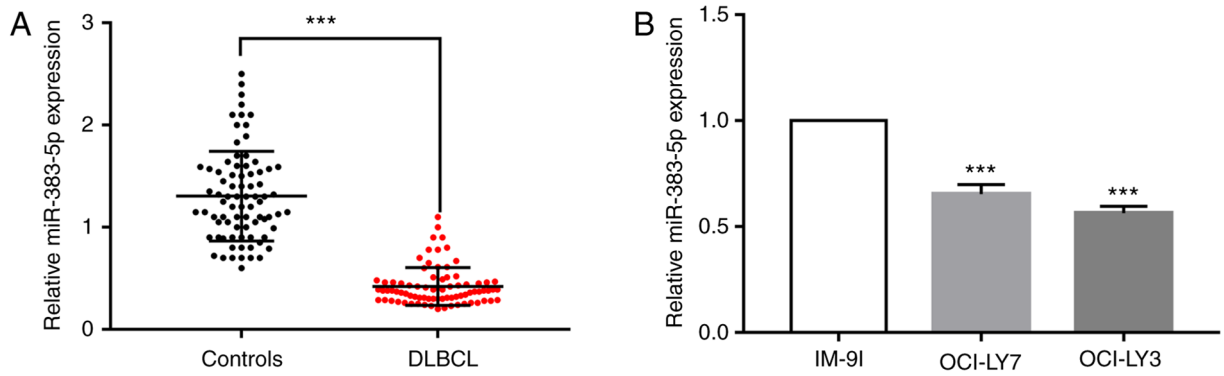

Figure 1. miR-383-5p expression is downregulated in DLBCL tissues and cell lines. (A) RT-qPCR analysis was performed to detect miR-383-5p expression in DLBCL tissues and control lymphoid hyperplasia tissues. (B) RT-qPCR analysis was performed to detect miR-383-5p expression in DLBCL cell lines (OCI-LY7 and OCI-LY3 cells) and normal B lymphocyte (IM-9I cells). Data are presented as the mean ± standard deviation (n=3). ***P<0.001. miR, microRNA; DLBCL, diffuse large B-cell lymphoma; RT-qPCR, reverse transcription-quantitative PCR.

fields using a light microscope (magnification, x200; Olympus Corporation).

Statistical analysis. Statistical analysis was performed using GraphPad Prism 5.0 software (GraphPad Software Inc.) and SPSS 20.0 software (IBM Corp.). All experiments were performed in triplicate and data are presented as the mean ± standard deviation. The χ^2 test was used to assess the association between miR-383-5p expression and the clinicopathological characteristics of patients with DLBCL. Unpaired Student's t-test was used to compare differences between two groups, while one-way ANOVA followed by LSD test were used to compare differences between multiple groups. Kaplan-Meier curves were generated for both OS and DFS. Cox regression analysis was performed to determine the prognostic factors. P<0.05 was considered to indicate a statistically significant difference.

Results

miR-383-5p expression is downregulated in DLBCL tissues and cell lines. RT-qPCR analysis was performed to detect miR-383-5p expression in 80 paired DLBCL tissues and normal tissues from patients with RLH. The results demonstrated that miR-383-5p expression was significantly downregulated in DLBCL tissues compared with RLH tissues (P<0.001; Fig. 1A). miR-383-5p expression was also detected in the DLBCL cell lines (OCI-LY7 and OCI-LY3 cells) and normal B lymphocytes (IM-9I cells). As presented in Fig. 1B, miR-383-5p expression was significantly lower in DLBCL cells compared with IM-9I cells (P<0.001).

Patients with DLBCL were classified into two groups, miR-383-5p low expression (n=40) and miR-383-5p high expression (n=40) groups, based on median miR-383-5p expression.

Association between miR-383-5p expression and the clinicopathological characteristics of patients with DLBCL. The association between miR-383-5p expression and the clinicopathological characteristics of patients with DLBCL was assessed. As presented in Table I, patients with low miR-383-5p expression were significantly associated with advanced clinical stages of the disease (P=0.004). In addition, low miR-383-5p expression was significantly associated with a higher rate of extranodal invasion compared with the high miR-383-5p expression group (P=0.001). Notably, no significant differences in age, sex, B symptoms, IPI score and serum LDH levels were observed between the two groups.

Kaplan-Meier survival analysis demonstrated that patients with high miR-383-5p expression had significantly higher OS (P=0.002; Fig. 2A) and DFS (P=0.04; Fig. 2B) rates than those with low miR-383-5p expression. Univariate and multivariate Cox regression analyses were performed to determine the prognostic factors associated with OS and DFS.

The prognostic factors found to be significant in the univariate analysis (P<0.05) were subjected to multivariate analysis with the Cox proportional hazards regression model. Univariate and multivariate analyses indicated that OS was significantly associated with clinical stage [hazard ratio (HR), 1.570; 95% confidence interval (CI), 1.402-1.759; P=0.001], extranodal invasion (HR, 1.444; 95% CI, 1.265-1.649; P=0.001) and miR-383-5p expression (HR, 0.844; 95% CI, 0.754-0.945; P=0.003) (Table II). Similarly, multivariate analysis indicated that DFS was significantly associated with clinical stage (HR, 1.605; 95% CI, 1.433-1.797; P<0.001), extranodal invasion (HR, 1.734; 95% CI, 1.520-1.981; P<0.001) and miR-383-5p expression (HR, 0.753; 95% CI, 0.672-0.842; P<0.001) (Table III).

Patients were classified into two groups, miR-383-5p high expression (n=20) and miR-383-5p low expression (n=60) groups, based on the 25th percentile. Kaplan-Meier survival analysis demonstrated that patients with high miR-383-5p expression had a significantly higher OS rate (P=0.032; Fig. 2C). However, no significant difference in DFS rate was observed between the two groups (P=0.217; Fig. 2D). Taken together, these results suggest that miR-383-5p expression is downregulated in patients with DLBCL, and high miR-383-5p expression is associated with a favorable clinical prognosis.

Overexpression of miR-383-5p inhibits the proliferation and invasion of DLBCL cells. The biological function of miR-383-5p during DLBCL progression was investigated. OCI-LY7 and OCI-LY3 cells were transfected with miR-383-5p mimic, and the effect of overexpressing miR-383-5p on the proliferation

Table I. Association between miR-383-5p expression and the clinicopathological characteristics of patients with diffuse large B-cell lymphoma (n=80).

Characteristic	Patients, n	miR-383-5p expression, n (%)		P-value
		High (n=40)	Low (n=40)	
Age, years				0.654
<60	38	18 (45.0)	20 (50.0)	
≥60	42	22 (55.0)	20 (50.0)	
Sex				0.072
Male	36	14 (35.0)	22 (55.0)	
Female	44	26 (65.0)	18 (45.0)	
B symptoms				0.653
Absent	36	19 (47.5)	17 (42.5)	
Present	44	21 (52.5)	23 (57.5)	
Clinical stage				0.004[a]
I/II	43	28 (70.0)	15 (37.5)	
III/IV	37	12 (30.0)	25 (62.5)	
Extranodal invasion				0.001[a]
<2	39	27 (57.5)	12 (20.0)	
≥2	41	13 (42.5)	28 (80.0)	
IPI score				0.651
0-2	34	18 (45.0)	16 (40.0)	
3-5	46	22 (55.0)	24 (60.0)	
Serum LDH level, IU/l				0.073
<300	38	23 (57.5)	15 (37.5)	
≥300	42	17 (42.5)	25 (62.5)	

[a]P<0.01. miR, microRNA; IPI, International Prognostic Index; LDH, lactate dehydrogenase.

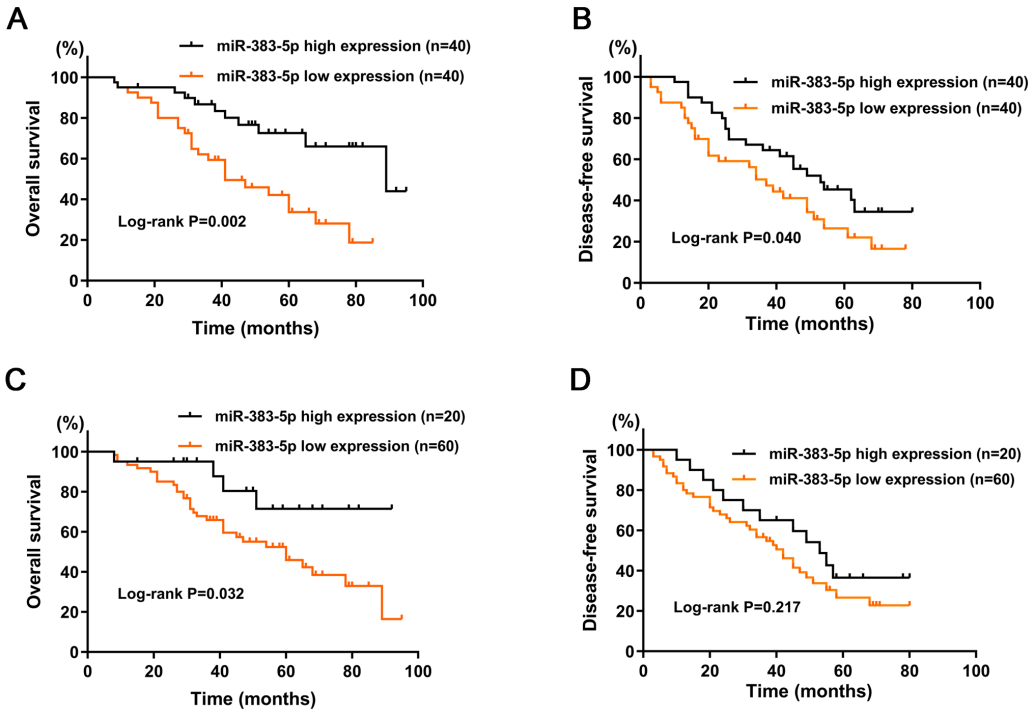

Figure 2. miR-383-5p expression is associated with the prognosis of patients with diffuse large B-cell lymphoma. Patients with high miR-383-5p expression had significantly higher (A) overall survival and (B) disease-free survival rates than those with low miR-383-5p expression. (C) Patients with high miR-383-5p expression had a significantly higher overall survival rate (D) but not disease-free survival rate than those with low miR-383-5p expression. miR, microRNA.

Table II. Univariate and multivariate analyses of prognostic factors associated with overall survival.

	Univariate		Multivariate	
Variable	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, years (≥60 vs. <60)	1.005 (0.841-1.200)	0.931	-	-
Sex (Male vs. Female)	1.036 (0.830-1.292)	0.755	-	-
B symptoms (Absent vs. Present)	0.923 (0.761-1.121)	0.419	-	-
Clinical stage (I/II vs. III/IV)	1.592 (1.422-1.782)	<0.001[b]	1.570 (1.402-1.759)	0.001[a]
Extranodal invasion (≥2 vs. <2)	1.448 (1.268-1.656)	<0.001[b]	1.444 (1.265-1.649)	0.001[a]
IPI score (3-5 vs. 0-2)	1.231 (0.686-2.423)	0.376	-	-
Serum LDH level, IU/l (≥300 vs. <300)	1.983 (0.881-3.123)	0.556	-	-
miR-383-5p expression (High vs. Low)	0.783 (0.700-0.876)	0.001[a]	0.844 (0.754-0.945)	0.003[a]

[a]P<0.01, [b]P<0.001. IPI, International Prognostic Index; LDH, lactate dehydrogenase; miR, microRNA; HR, hazard ratio; CI, confidence interval; -, not available.

Table III. Univariate and multivariate analyses of prognostic factors associated with disease-free survival.

	Univariate		Multivariate	
Variable	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, years (≥60 vs. <60)	1.163 (0.960-1.411)	0.112	-	-
Sex (Male vs. Female)	1.009 (0.845-1.206)	0.920	-	-
B symptoms (Absent vs. Present)	1.006 (0.878-1.152)	0.931	-	-
Clinical stage (I/II vs. III/IV)	1.570 (1.402-1.757)	<0.001[a]	1.605 (1.433-1.797)	<0.001[a]
Extranodal invasion (≥2 vs. <2)	1.701 (1.490-1.944)	<0.001[a]	1.734 (1.520-1.981)	<0.001[a]
IPI score (0-2 vs. 3-5)	1.056 (0.931-1.197)	0.398	-	-
Serum LDH level (≥300 vs. <300)	1.068 (0.927-1.230)	0.365	-	-
miR-383-5p expression (High vs. Low)	0.726 (0.649-0.812)	<0.001[a]	0.753 (0.672-0.842)	<0.001[a]

[a]P<0.001. IPI, International Prognostic Index; LDH, lactate dehydrogenase; miR, microRNA; HR, hazard ratio; CI, confidence interval; -, not available.

and invasion of lymphoma cells was assessed *in vitro*. The results confirmed that miR-383-5p mimic significantly increased miR-383-5p expression in OCI-LY7 and OCI-LY3 cells (P<0.001; Fig. 3A and B).

The results of the CCK-8 assay demonstrated that the number of OCI-LY7 and OCI-LY3 cells significantly decreased at days 3 and 4 following transfection with miR-383-5p mimic compared with the untreated cells (P<0.01 and P<0.001; Fig. 3C and D). In addition, crystal violet staining demonstrated that overexpression of miR-383-5p significantly inhibited the proliferation of both OCI-LY7 and OCI-LY3 cells (P<0.001; Fig. 3E). The results of the Transwell assay demonstrated that overexpression of miR-383-5p significantly inhibited the invasive ability of both OCI-LY7 and OCI-LY3 cells (P<0.001; Fig. 3F).

miR-383-5p knockdown promotes the proliferation and invasion of DLBCL cells. OCI-LY7 and OCI-LY3 cells were transfected with miR-383-5p inhibitor to decrease miR-383-5p expression, and the results indicated that miR-383-5p inhibitor markedly suppressed miR-383-5p expression in OCI-LY7 and OCI-LY3 cells (P<0.001; Fig. 4A and B). The results of the CCK-8 assay and crystal violet staining demonstrated that miR-383-5p knockdown significantly promoted the proliferative ability of both OCI-LY7 and OCI-LY3 cells (P<0.05 Fig. 4C-E). Similarly, the results of the Transwell assay demonstrated that miR-383-5p knockdown significantly promoted the invasive ability of OCI-LY7 and OCI-LY3 (P<0.001; Fig. 4F).

Discussion

Several miRNAs have been demonstrated to play fundamental roles in the initiation and progression of DLBCL. For example, miR-155 knockdown inhibits cell proliferation and facilitates apoptosis of DLBCL *in vitro* by upregulating *SOCS3* expression to suppress JAK-STAT3 signaling (27). In addition, low miR-27b expression is associated with poor overall survival of patients with DLBCL, while high miR-27b expression suppresses the proliferation of DLBCL cells (28).

The results of the present study demonstrated that miR-383-5p expression was downregulated in human DLBCL tissues and related cell lines. In addition, miR-383-5p

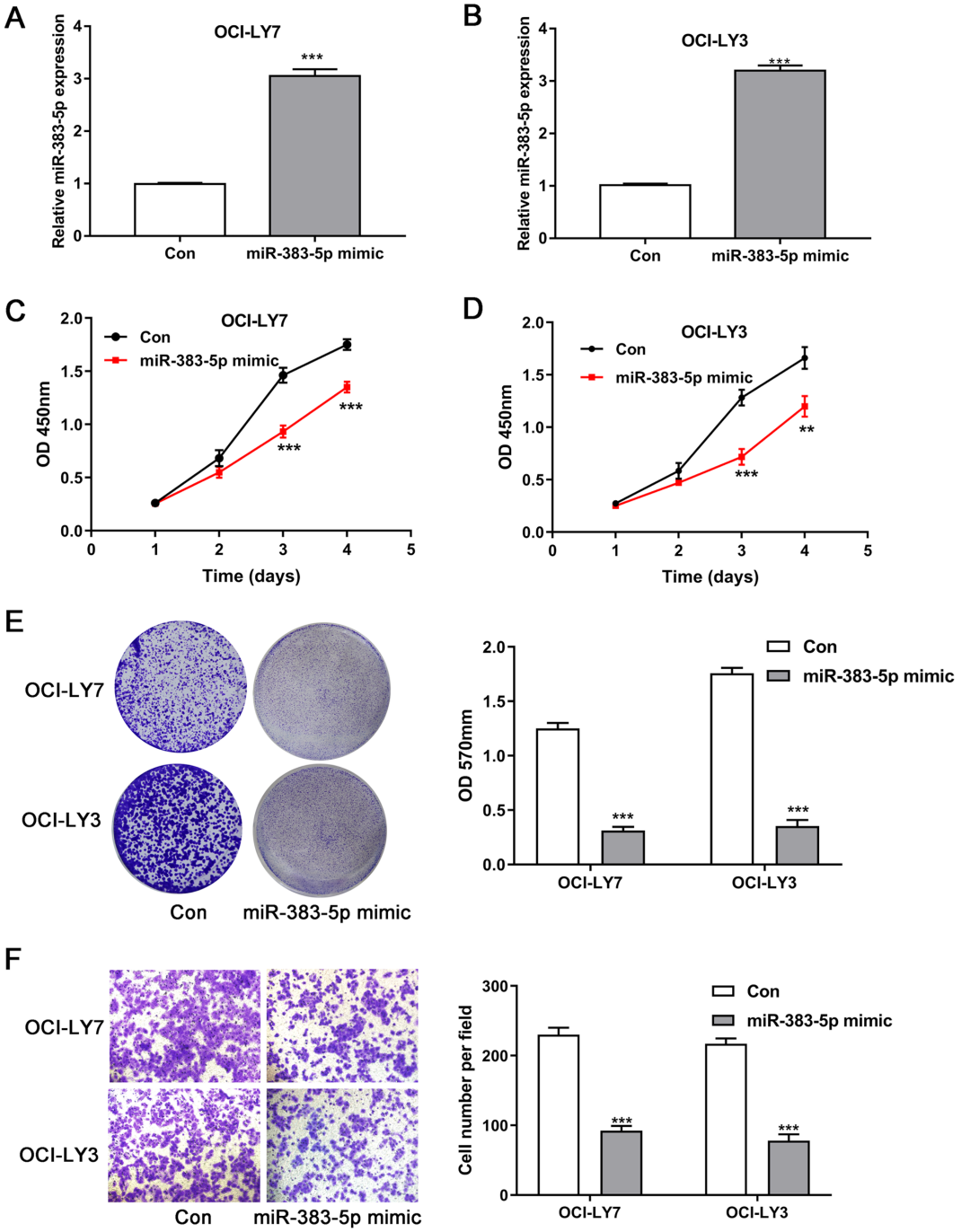

Figure 3. Overexpression of miR-383-5p inhibits the proliferation and invasion of diffuse large B-cell lymphoma cells. miR-383-5p expression was detected in (A) OCI-LY7 and (B) OCI-LY3 cells following transfection with miR-383-5p mimic and negative control, respectively. The Cell Counting Kit-8 assay was performed to assess the effect of miR-383-5p overexpression on the proliferative ability of (C) OCI-LY7 and (D) OCI-LY3 cells. (E) Crystal violet staining was performed to assess the effect of miR-383-5p overexpression on the proliferation of OCI-LY7 and OCI-LY3 cells. (F) The Transwell assay was performed to assess the effect of miR-383-5p overexpression on the invasive ability of OCI-LY7 and OCI-LY3 cells (magnification, x200). Data are presented as the mean ± standard deviation (n=3). **P<0.01, ***P<0.001 vs. Con. miR, microRNA; Con, control; OD, optical density.

expression was closely associated with advanced clinical stage and extranodal invasion. Notably, high miR-383-5p expression predicted favorable clinical prognosis for patients with DLBCL. Taken together, these results suggest that miR-383-5p may serve as an independent prognostic biomarker, as well as a tumor suppressor in patients with DLBCL. Overexpression and knockdown of miR-383-5p were performed in two independent DLBCL cell lines using miR-383-5p mimic and inhibitor, respectively. The effect of altering miR-383-5p expression on the proliferation and invasion of DLBCL cells was assessed. The results demonstrated that overexpression of miR-383-5p significantly inhibited the proliferation and invasion of DLBCL cells, the effects of which were reversed following miR-383-5p knockdown.

The tumor suppressive role of miR-383-5p has been reported in several malignancies, including breast (15), gastric (16) and ovarian cancers (18), as well as lung adenocarcinoma (19). Zhang *et al* (15) demonstrated that miR-383-5p

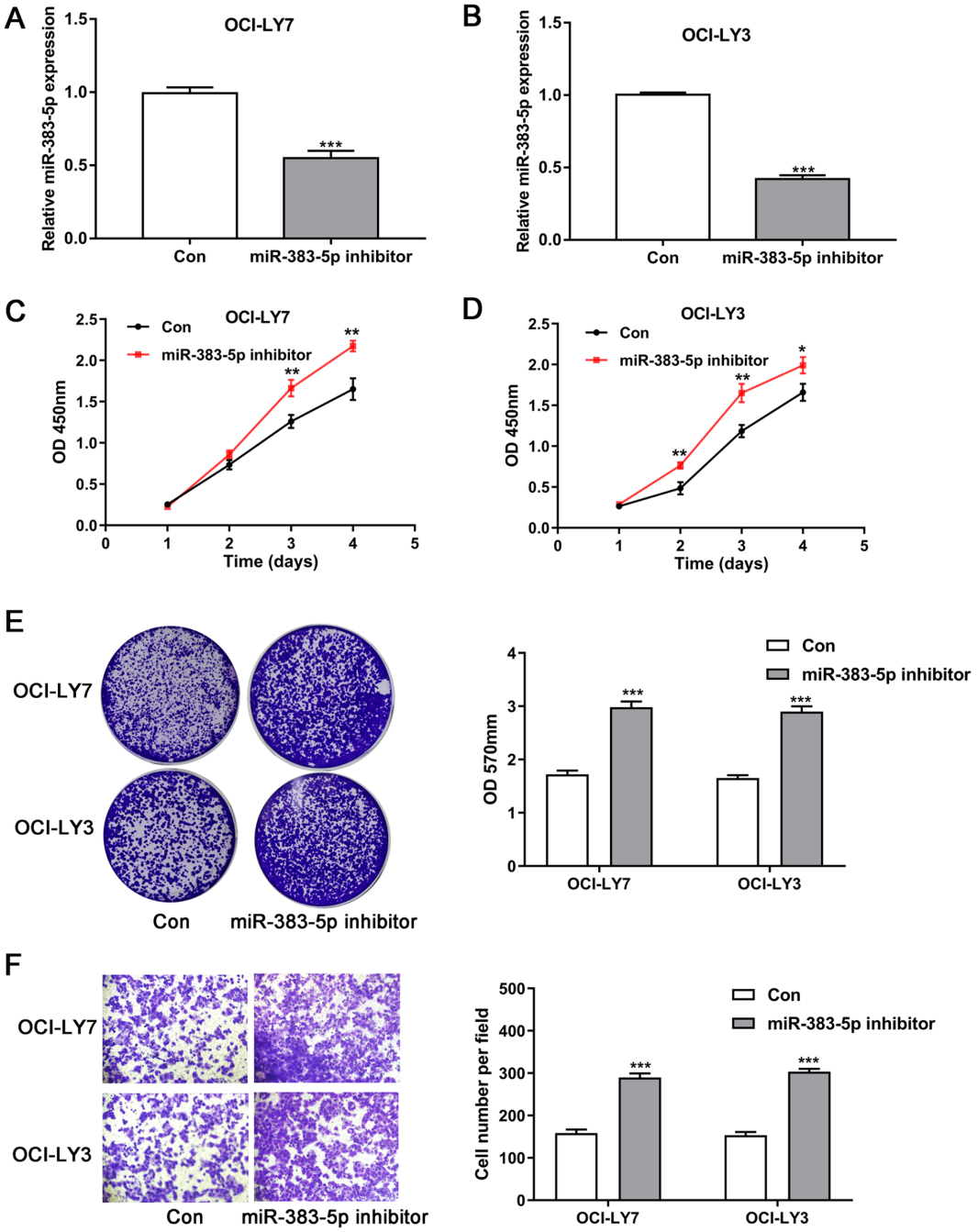

Figure 4. miR-383-5p knockdown promotes the proliferation and invasion of diffuse large B-cell lymphoma cells. miR-383-5p expression was detected in (A) OCI-LY7 and (B) OCI-LY3 cells following transfection with miR-383-5p inhibitor and negative control, respectively. The Cell Counting Kit-8 assay was performed to assess the effect of miR-383-5p knockdown on the proliferative ability of (C) OCI-LY7 and (D) OCI-LY3 cells. (E) Crystal violet staining was performed to assess the effect of miR-383-5p knockdown on the proliferation of OCI-LY7 and OCI-LY3 cells. (F) The Transwell assay was performed to assess the effect of miR-383-5p knockdown on the invasive ability of OCI-LY7 and OCI-LY3 cells (magnification, x200). Data are presented as the mean ± standard deviation (n=3). *P<0.05, **P<0.01, ***P<0.001 vs. Con. miR, microRNA; Con, control; OD, optical density.

expression is downregulated in breast cancer tissues and respective cell lines. In addition, miR-383-5p can inhibit the proliferation, migration and invasion of breast cancer cells, the findings of which are consistent with the results of the present study. Xu *et al* (17) reported that overexpression of miR-383-5p suppresses the proliferation and increases the apoptosis of gastric cancer cells, suggesting its prominent role in gastric carcinogenesis. In addition, overexpression of miR-383-5p inhibits cell proliferation, tumor growth and enhances chemosensitivity of ovarian cancer cells by downregulating *TRIM27* expression (18). miR-383-5p expression is downregulated in lung adenocarcinoma tissues, and also exerts antiproliferative effects on lung adenocarcinoma cells (19). Further studies are required to determine the underlying mechanism of miR-383-5p in regulating the progression of DLBCL cells.

In conclusion, the results of the present study demonstrated that miR-383-5p expression is downregulated in DLBCL tissues, and thus may serve as a prognostic biomarker for patients with DLBCL. In addition, miR-383-5p appears to play

a critical role in inhibiting the proliferation and invasion of DLBCL cells, and thus may act as a putative therapeutic target for effective treatment of DLBCL.

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Availability of data and materials

All data generated or analyzed during the present study are included in this published article.

Authors' contributions

LYC, BQH and XMZ designed the present study, performed the experiments and analyzed the data. XBY, DDY and LQY collected the clinical samples and analyzed the data. LYC and LQY confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent for participation

The present study was approved by the Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (Harbin, China; approval no. ASHHM000152), and performed in accordance with the Declaration of Helsinki. Written informed consent was provided by all patients prior to the study start.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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