miR-1297 promotes apoptosis and inhibits the proliferation and invasion of hepatocellular carcinoma cells by targeting *HMGA2*

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Received January 24, 2015; Accepted August 14, 2015

DOI: 10.3892/ijmm.2015.2341

Abstract. MicroRNAs (miRNAs) have recently emerged as important regulators of gene expression in various tissues. In particular, miRNAs have been identified as new therapeutic agents and biomarkers in cancer. The aim of the present study was to explore whether *miR-1297* has an anti-cancer role in hepatocellular carcinoma cell lines and to explore its underlying mechanism. The proliferation, apoptosis and migration of hepatocellular carcinoma cells were evaluated by cell viability assay, TUNEL staining and a wound healing assay, respectively. Western blot analysis and reverse transcription polymerase chain reaction (RT-PCR) were performed to determine the expression levels of proteins and mRNAs of high-mobility group AT-hook 2 (HMGA2) in hepatocellular carcinoma. The luciferase assay was employed to verify the inhibitory activity of *miR-1297* on the 3' untranslated region (3'UTR) of the *HMGA2* gene. In the present study, overexpression of *miR-1297* significantly inhibited the proliferation of HepG2 and SMMC7721 cells. Forced expression of *miR-1297* also increased the apoptosis of HepG2 and SMMC7721. Furthermore, the migration of HepG2 and SMMC7721 was also clearly suppressed by *miR-1297* overexpression. All these effects can be abrogated by co-transfection with *miR-1297* inhibitor-AMO-1297. The luciferase assay verified that *miR-1297* overexpression is able to inhibit the activity of luciferase reporter harboring the *HMGA2* 3'UTR, indicating *HMGA2* as the target of *miR-1297*. Although the *HMGA2* level was not affected by *miR-1297*, the HMGA2 protein was significantly inhibited by *miR-1297* overexpression. Collectively, *miR-1297* was revealed to regulate the proliferation, apoptosis and migration of hepatocellular carcinoma cells via acting on HMGA2. The finding provides a new target for the treatment of hepatocellular carcinoma.

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Key words: miR-1297, migration, high-mobility group AT-hook 2, hepatocellular carcinoma, apoptosis

Introduction

Hepatocellular carcinoma remains the most common type of liver cancer, and usually develops secondary to cirrhosis or viral hepatitis infection. The incidence of hepatocellular carcinoma has gradually increased in certain developed and developing countries. Despite advances in multidisciplinary therapies, the median survival time of patients with hepatocellular carcinoma is ~9 months (1). Therefore, the characterization of molecular mechanisms underlying the initiation and progress of hepatocellular carcinoma is necessary. Certain factors, including inflammation, oxidative stress and hypoxia, have been shown to facilitate the initiation, progression and metastasis of hepatocellular carcinoma (2). The androgen receptor has been reported to regulate cell adhesion and migration of hepatocellular carcinoma via regulating the β1-integrin-AKT signaling pathway (3). Overexpression of actopaxin may lead to the increase of invasion and migration ability, and an epithelial-mesenchymal transition process in hepatocellular carcinoma (4). mTOR signaling was also shown to have a critical role in the pathogenesis of hepatocellular carcinoma (5). Oxysterol-binding protein (OSBP)-related protein 8 (ORP8) markedly inhibited tumor growth and induced cell apoptosis of hepatocellular carcinoma cells through the Fas/FasL pathway *in vivo* and *in vitro* (6).

MicroRNAs (miRNA) have been recognized as potential therapeutic targets for hepatocellular carcinoma. miRNAs are a class of small non-coding RNA molecules and post-transcriptionally regulate protein expression by targeting the 3' untranslated region (3'UTR) of target mRNA, causing degradation or repression of translation (7). Previous studies have reported that miRNAs have important roles in the development and maintenance of various diseases, such as cancer, heart hypertrophy and fibrosis (8-11). For example, in hearts, the upregulation of *miR-23a* induced by isoproterenol or aldosterone caused hypertrophic growth of cardiomyocytes, and the knockdown of *miR-23a* could attenuate cardiomyocyte hypertrophy by regulating NFATc3 (12). Particularly in cancer, miRNAs have emerged as new potential therapeutic molecules

and targets (13,14). The *miR-543* level was significantly reduced in hepatocellular carcinoma, and overexpression of *miR-543* enhanced the proliferation and invasion of HepG2 via targeting PAQR3 in hepatocellular carcinoma (13). Additionally, *miR-520e* can inhibit the growth of hepatocellular carcinoma cells, and the knockdown of *miR-520e* lead to increased cell proliferation (14). Overexpression of *miR-375* reduced cell proliferation and migration, and also induced G_1 arrest and apoptosis in hepatocellular carcinoma cells via targeting at AEG-1 (15). *miR-1* has been shown to promote apoptosis of HepG2 by targeting apoptosis inhibitor-5 (16). It was previously reported that *miR-1297* exerted antitumor effects on human lung adenocarcinoma cell and colorectal cancer (17,18), and acted as a tumor suppressor. However, whether *miR-1297* has an inhibitory effect on hepatocellular carcinoma has not been determined.

To the best of our knowledge, the present study established for the first time, a potential association between *miR-1297* and the proliferation, apoptosis and migration of hepatocellular carcinoma cells. The antitumor effects of *miR-1297* on HepG2 and SMMC7721 cells were investigated, and the precise mechanism of *miR-1297* was explored in inhibiting liver cancer.

Materials and methods

Reagents. Dulbecco's modified Eagle's medium (DMEM), fetal bovine serum (FBS) and phosphate-buffered saline (PBS) were purchased from HyClone Laboratories. Lipofectamine™ 2000 was purchased from Invitrogen (Carlsbad, CA, USA). Hsa-*miR-1297* mimics (*miR-1297*), hsa-*miR-1297* inhibitor (AMO-1297) and its scramble negative control (control) were synthesized by Sangon (Shanghai, China). Unless otherwise specified, all the other reagents were purchased from Sigma Chemical Co. (St. Louis, MO, USA).

Cell culture. Human hepatocellular carcinoma HepG2 and SMMC7721 cell lines were purchased from the China Center for Type Culture Collection (Wuhan, China). These two cell lines were cultured in DMEM supplemented with 10% FBS and penicillin (100 U/ml)/streptomycin (100 μg/ml), and were subsequently transferred into plastic culture flasks and cultured at 37˚C in humid air with 5% CO_2.

miRNAs transfection. miRNAs were transected into HepG2 and SMMC7721 at 50-70% confluence using Lipofectamine 2000 reagent according to the manufacturer's instructions. The final oligonucleotide concentration of *miR-1297*, AMO-1297 or its scramble reached 50 nmol/l. Three hours after miRNAs transfection, the culture medium was changed to fresh DMEM with 10% FBS. Subsequently, HepG2 and SMMC7721 were incubated for an additional 48 h and harvested for further investigation. These transfected oligonucleotides were divided into four groups: Control, hsa-*miR-1297* mimics (*miR-1297*), hsa-*miR-1297* + hsa-*miR-1297* inhibitor (miR-1297 + AMO-1297) and its scramble negative control (scramble).

Cell viability assay. Cell viability of HepG2 and SMMC7721 was determined by the MTT assay, according to the methods described in a previous study (14). In brief, HepG2 and SMMC7721 cells were seeded in 96-well plates, and were transfected with *miR-1297*, *miR-1297* + AMO-1297 or its scramble. After transfection, the cells were exposed to 10 μl of MTT solution (5 mg/ml) for 2-4 h at 37˚C. After the supernatant was removed from formazan crystals, and dimethyl sulfoxide (DMSO) was added. The cell viability was calculated according to the absorbance at 570 nm using an OPTImax microplate reader.

Terminal deoxynucleotidyltransferase-mediated dUTP nick end labelling (TUNEL) assay. Apoptosis of HepG2 and SMMC7721 cells was determined using a TUNEL detection kit (Roche, Penzberg, Germany) according to the manufacturer's instructions. After transfection with *miR-1297*, *miR-1297* + AMO-1297 or its scramble, HepG2 and SMMC7721 cells were fixed with 4% paraformaldehyde in PBS for 1 h at room temperature, and permeabilized with 0.1% Triton X-100 in 0.1% sodium citrate for 2 min on ice. Following washing in PBS, sections were incubated with the TUNEL reaction mixture for 1 h at 37˚C. After washing with PBS, the stained cells were visualized using a fluorescence microscope (Eclipse TE300; Nikon, Tokyo, Japan).

Wound healing assay. HepG2 and SMMC7721 cells were cultured in a 6-well plate for 24 h. The wound healing assay was carried out by introducing a small linear scratch with a pipette tip. Subsequently, the cells in each well were incubated with serum-free DMEM medium. Images of 48 h following the scratch in cultured cells were captured under a phase-contrast microscope (magnification, x200) to monitor the cell migration process.

Transwell assay. The Transwell assay was performed using a Transwell chamber with pore size of 8.0 μm (Millipore, Billerica, MA, USA). The cells were resuspended in serum-free medium and were placed in the upper chamber in 5% CO_2 at 37˚C. Following transfection, cultured HepG2 and SMMC7721 cells in the upper chamber were removed, and the attached cells in the lower section were stained with 0.1% crystal violet. The migration rate was quantified by counting the migration cells in six random fields under a light microscope.

Bioinformatics predication. The potential target gene of *miR-1297* was predicted by computer-aided algorithms using TargetScan (http://www.targetscan.org).

Luciferase reporter assay. After plating in a 24-well plate, HEK293 cells were transfected with the constructed reporter plasmid containing 3'UTR of high-mobility group AT-hook 2 (HMGA2) plus *miR-1297*, *miR-1297* + AMO-1297 or its scramble. Luciferase assays were performed using the Dual-Luciferase Reporter Assay system (Promega, Madison, WI, USA) 24 h after transfection.

RNA extraction and reverse transcripion-quantitative polymerase chain reaction (RT-qPCR) analysis. Total RNA was extracted from the cells using TRIzol according to the manufacturer's instructions. RT-qPCR was conducted using an RT-PCR kit (Takara, Dalian, China). The primers used were

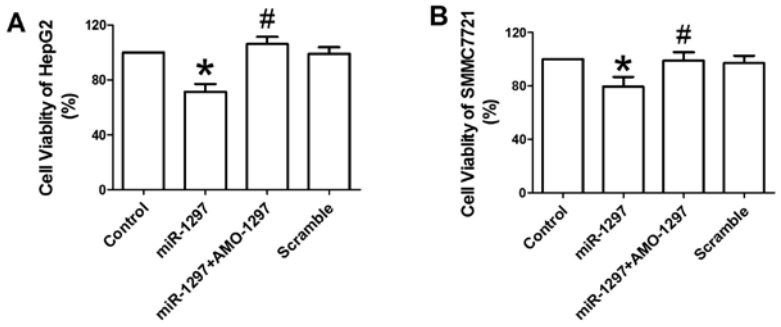

Figure 1. Effect of *miR-1297* overexpression on the cellular viability of HepG2 and SMMC7721 cells. (A) HepG2 and (B) SMMC7721 cell proliferation following *miR-1297*, *miR-1297* + AMO-1297 and its scramble transfection, as measured by the MTT assay. Overexpression of *miR-1297* inhibited the proliferation of HepG2 and SMMC7721 cells, which can be abrogated by co-transfection of AMO-1297. Data are expressed as mean ± standard error of the mean. N=5. *P<0.05 vs. control; #P<0.05 vs. *miR-1297*.

all synthesized by Sangon. Semi-quantitative RT-PCR was performed using a thermal cycler (Bio-Rad, Hercules, CA, USA). The primer sequences for human *HMGA2* gene expression were as follows: *HMGA2* forward, 5'-TGGGAGGA GCGAAATCTAAA-3' and reverse, 5'-AAGCACCTTG GTCAACCATC-3'; and β-actin forward, 5'-TGAAGATCAA GATCATTGCTCC-3' and reverse, 5'-GCCATGCCAAT CTCATCTTG-3'. The relative *HMGA2* mRNA levels were normalized to those of β-actin mRNA levels using Quality One analysis software (Bio-Rad).

Western blot analysis. The protein samples were extracted from the cultured HepG2 and SMMC7721 cells. After 12,000 x g centrifugation at 4˚C for 10 min, the concentration of extracted protein was determined by the bicinchoninic acid method (Beyotime, Jiangsu, China). The extracted proteins were separated using 10-12% sodium dodecyl sulfate-polyacrylamide gel electrophoresis and subsequently electrophoretically transferred to the PVDF membrane (Millipore). The membranes were blocked in blocking buffer (5% non-fat milk dissolved in PBS-Tween-20) overnight at 4˚C. Subsequently, the membranes were incubated with goat polyclonal antibodies against HMGA2 (sc-23684) and mouse monoclonal anti-glyceraldehyde 3-phosphate dehydrogenase (GAPDH) antibody (sc-32233; Santa Cruz Biotechnology, Inc., Dallas, TX, USA). The bands were visualized by ECL (Santa Cruz Biotechnology, Inc.) and detected by ECL Detection Systems (Thermo Scientific, Waltham, MA, USA). The GAPDH protein was used as an internal control.

Statistical analysis. Statistical data are shown as mean ± standard error of the mean. All the statistical analysis was performed by SPSS 13.0 software (SPSS, Inc., Chicago, IL, USA). Differences between two groups were defined with a t-test, and the significant differences among three groups were determined using analysis of variance. P<0.05 was considered to indicate a statistically significant difference.

Results

miR-1297 reduces the cellular viability of HepG2 and SMMC7721 cells. To evaluate the effects of *miR-1297* on the proliferation of HepG2 and SMMC7721 cells, the MTT assay was used to measure the cellular viability of HepG2 and SMMC7721. The overexpression of *miR-1297* resulted in a significant reduction of cellular viability in HepG2 cells compared with the control (P<0.05) (Fig. 1A). Co-transfection with AMO-1297 may abolish the inhibitory effects of *miR-1297* on the viability of HepG2 cells (P<0.05) (Fig. 1A). The scrambled negative control did not affect the viability of HepG2 cells. A similar anti-proliferation action of *miR-1297* was also observed in SMMC7721 cells (Fig. 1B). These results suggest that *miR-1297* has an inhibitory role in the proliferation of HepG2 and SMMC7721 cells.

miR-1297 induces the apoptosis of HepG2 and SMMC7721 cells. Whether *miR-1297* overexpression was able to induce apoptosis of HepG2 and SMMC7721 cells was further studied. The TUNEL assay was carried out to investigate the influence of *miR-1297* on the apoptosis of HepG2 and SMMC7721 cells. Fig. 2A demonstrates that *miR-1297* overexpression induced a significant increase of HepG2 cells that were positive for TUNEL staining compared with the control (P<0.05). Similarly, the number of HepG2 cells positive for TUNEL staining was also increased by *miR-1297* overexpression in SMMC7721 cells (P<0.05) (Fig. 2C). Co-transfection with AMO-1297 may suppress the increase of apoptosis by *miR-1297* in HepG2 and SMMC7721 cells (Fig. 2). The scrambled negative control did not significantly induce the apoptosis of HepG2 and SMMC7721 cells.

miR-1297 inhibits the migration of HepG2 and SMMC7721 cells. In addition to cellular proliferation, the effect of *miR-1297* on the migration activity of HepG2 and SMMC7721 cells was examined. The wound healing assay *in vitro* was carried out to determine cell migration of HepG2 and SMMC7721. Fig. 3A shows the quantified wound closure in cultured HepG2 cells following *miR-1297*, co-transfection with AMO-1297 and its scramble transfection. Wound closure was significantly slowed in *miR-1297*-treated HepG2 and SMMC7721 cells at 48 h after the scratch, compared with the control group (Fig. 3B and C). Consistently, the Transwell migration assay was also performed in HepG2 and SMMC7721 cells with *miR-1297*, co-transfection with AMO-1297 and its scramble transfection. In agreement with the wound healing assay, transfection with *miR-1297* overexpression produced

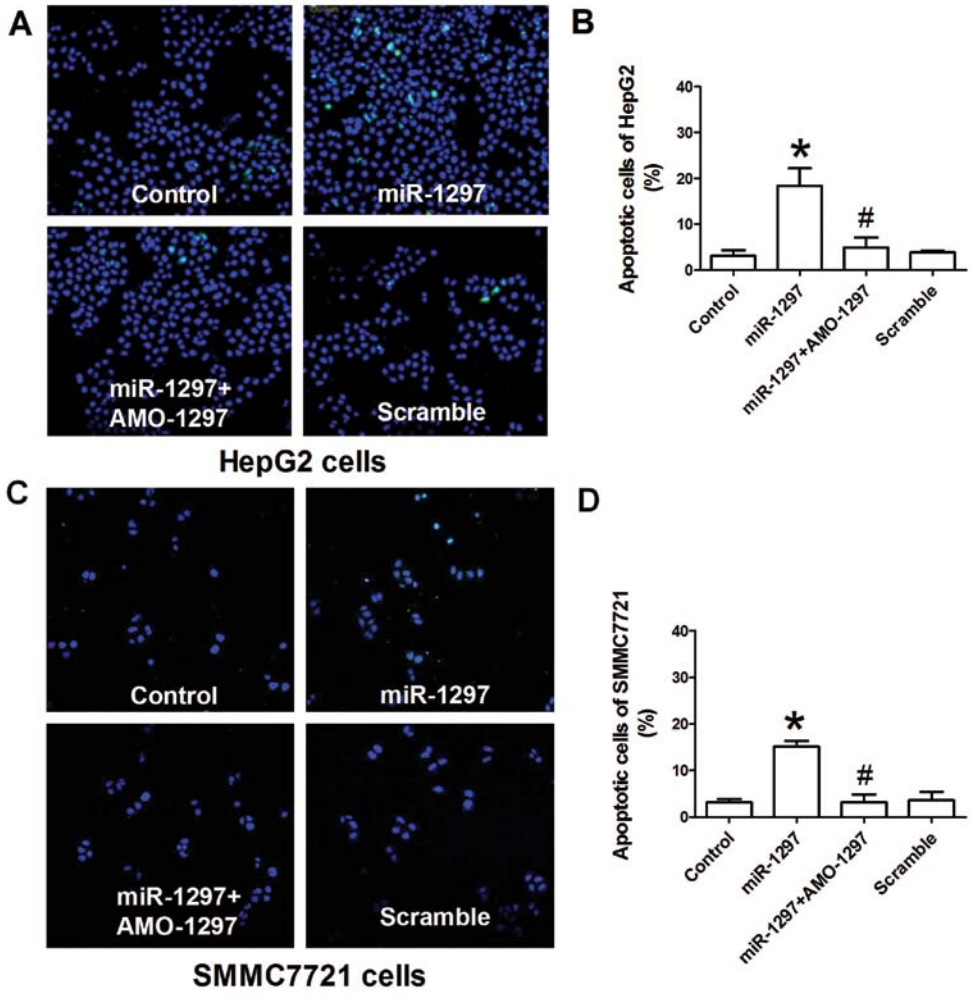

Figure 2. Effect of *miR-1297* on the apoptosis of HepG2 and SMMC7721 cells. (A) The representative images of terminal deoxynucleotidyltransferase-mediated dUTP nick end labelling (TUNEL)-positive HepG2 cells transfected with *miR-1297*, *miR-1297* + AMO-1297 and its scramble. (B) Statistical analysis of apoptotic HepG2 cells following transfection of *miR-1297*, *miR-1297* + AMO-1297 and its scramble. (C) The representative images of TUNEL-positive SMMC7721 cells following *miR-1297*, *miR-1297* + AMO-1297 and its scramble transfection. (D) *miR-1297* induced the increase of apoptotic SMMC7721 cells, and co-transfection with AMO-1297 abolished this change. Data are expressed as mean ± standard error of the mean. N=5. *P<0.05 vs. control; $^{\#}$P< 0.05 vs. *miR-1297*.

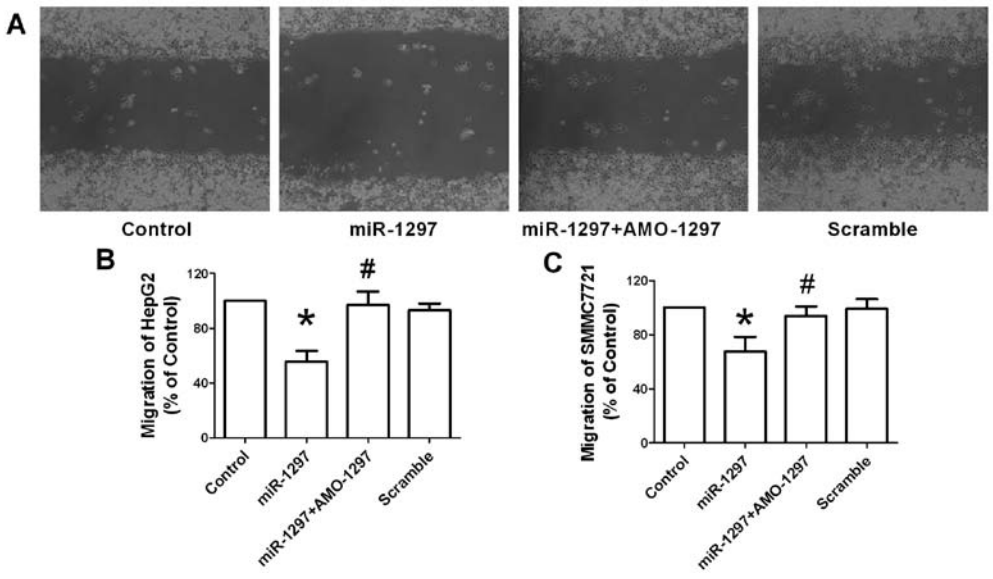

Figure 3. Effect of *miR-1297* on the migration of HepG2 and SMMC7721 cells by the wound healing assay. (A) Representative images of HepG2 cells of four groups following the scratch. (B) Statistical analysis of wound width of HepG2 cells with the transfection of *miR-1297*, *miR-1297* + AMO-1297 and its scramble. (C) Wound healing assay showed the inhibitory effects of *miR-1297* on the migration of SMMC7721 cells. Data are expressed as mean ± standard error of the mean. N=3. *P<0.05 vs. control; $^{\#}$P<0.05 vs. *miR-1297*.

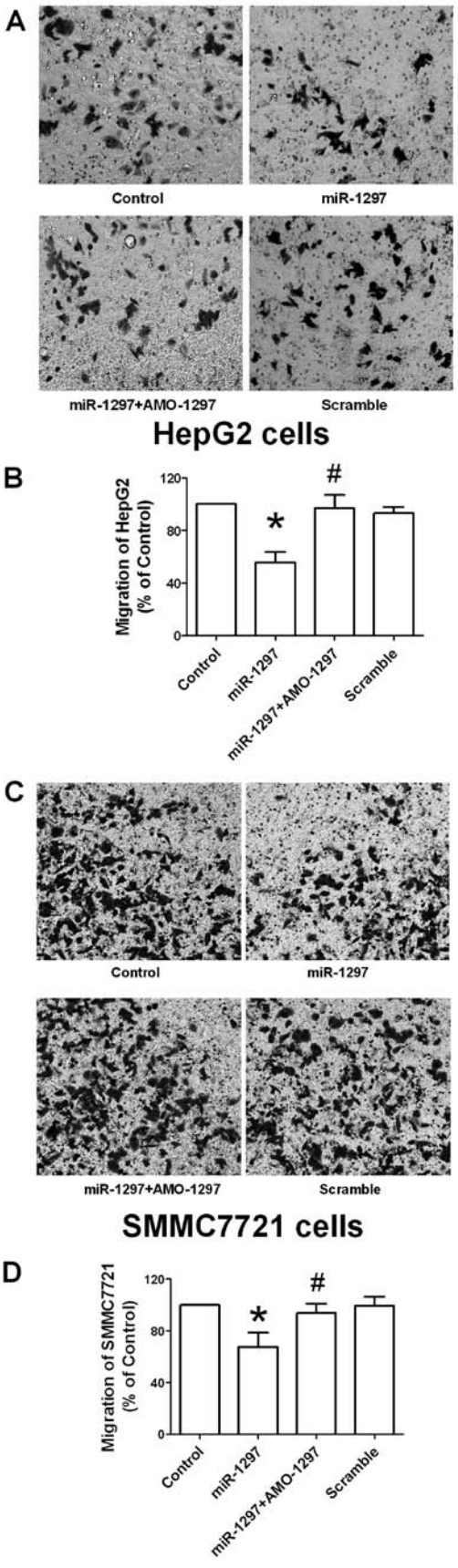

Figure 4. Effect of *miR-1297* on migration of HepG2 and SMMC7721 cells by the Transwell assay. (A and C) Representative images of HepG2 and SMMC7721 cells migrating through an 8.0 μm pore size membrane, respectively. (B and D) Statistical analysis of migrated HepG2 and SMMC7721 cells following the transfection of *miR-1297*, *miR-1297* + AMO-1297 and its scramble. Data are expressed as mean ± standard error of the mean. N=3. *P<0.05 vs. control; #P<0.05 vs. *miR-1297*.

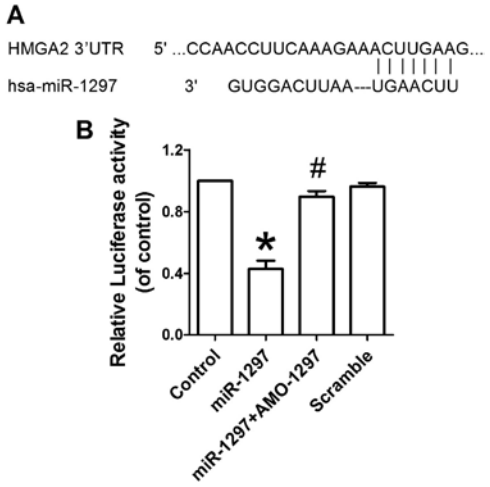

Figure 5. High-mobility group AT-hook 2 (HMGA2) is the target of *miR-1297*. (A) Schematic diagram of the putative *miR-1297* binding site in the 3' untranslated region (3'UTR) of HMGA2. (B) Relative luciferase activities of the reporter containing HMGA2 3'UTR were measured following transfection with *miR-1297*, AMO-1297 and its scramble, and are shown as the ratio of Firefly/*Renilla* activities in the cells and normalized to those of the control. Data are expressed as mean ± standard error of the mean. N=6. *P<0.05 vs. control; #P<0.05 vs. *miR-1297*.

an inhibition of migration of HepG2 (Fig. 4A and B) and SMMC7721 cells (Fig. 4C and D). This data demonstrated that the suppression of migration of hepatocellular carcinoma cells was induced by *miR-1297*.

miR-1297 targets the 3'UTR of HMGA2. A bioinformatics database of miRNAs was used (http://www.targetscan.org/) to predict the potential target gene of *miR-1297*. *miR-1297* was shown to have a putative binding site to the 3'UTR region of *HMGA2* (Fig. 5A). A highly conservative *miR-1297* binding site at the *HMGA2* 3'UTR 1867-1873 base position was predicted in humans. Subsequently, the Dual-Luciferase reporter assay was performed to confirm that *miR-1297* directly targeted the 3'UTR of *HMGA2*. Overexpression of *miR-1297* decreased the luciferase activity of the reporter plasmid harboring *HMGA2* 3'UTR, suggesting that *miR-1297* inhibits the translation of *HMGA2* by binding to its 3'UTR (Fig. 5B). However, co-transfection of AMO-1297 alleviated the reduction in luciferase activity caused by *miR-1297* in HEK293. These results indicate that *HMGA2* is a direct target of *miR-1297*.

miR-1297 regulates HMGA2 expression in hepatocellular carcinoma. Regulatory effects of *miR-1297* on *HMGA2* expression were further confirmed. *miR-1297*, *miR-1297* + AMO-1297 or its scramble were transfected into HepG2 and SMMC7721 cells, and western blotting was subsequently used to determine the level of HMGA2 protein. Fig. 6 demonstrates that the overexpression of *miR-1297* caused a significant reduction of HMGA2 protein in HepG2 and SMMC7721 cells compared with control (P<0.05). By contrast, co-transfection with AMO-1297 significantly reversed the reduction of the HMGA2 protein following *miR-1297* transfection (P<0.05). Transfection of scramble sequence did not affect the expression of HMGA2 protein in HepG2 and SMMC7721

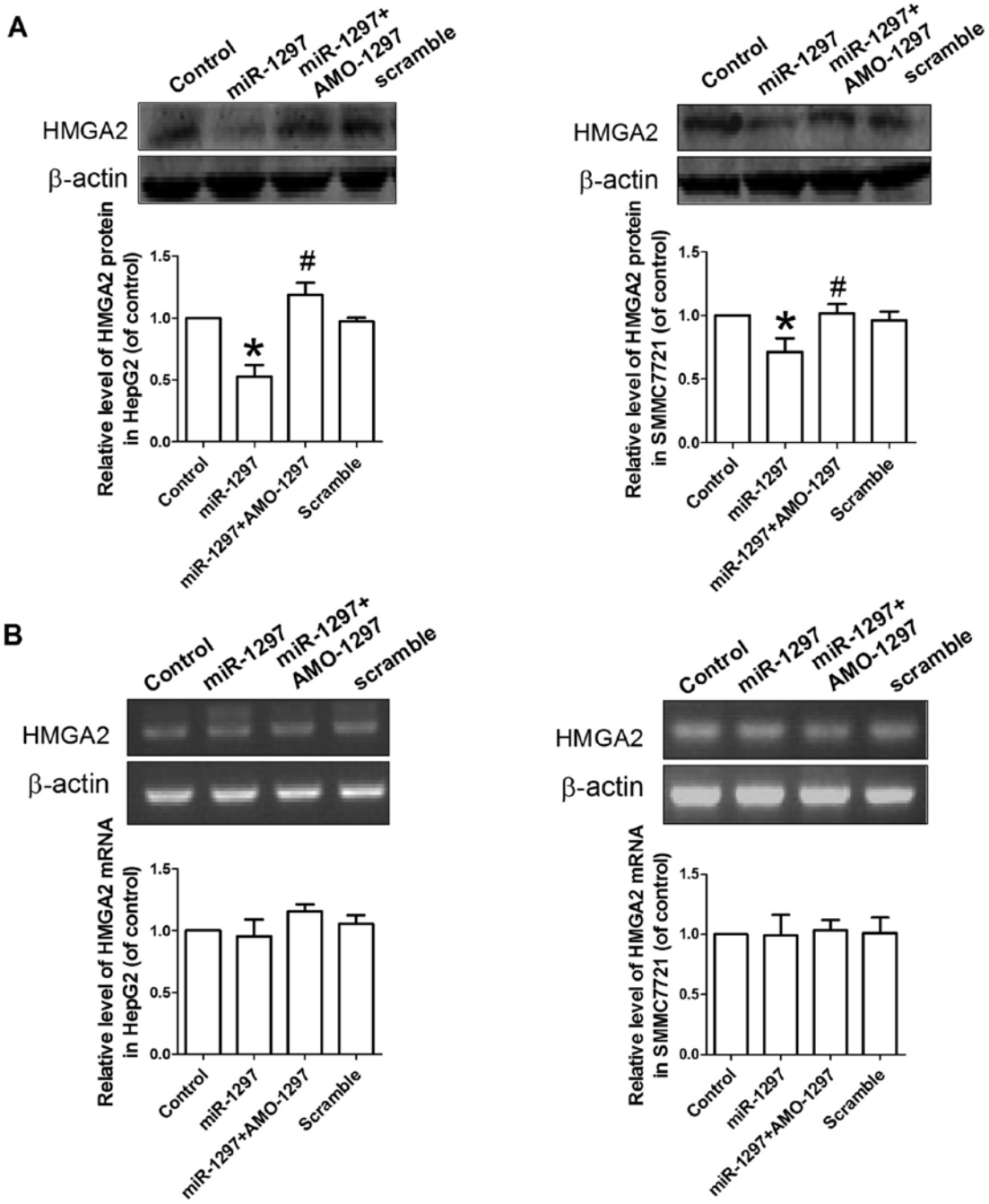

Figure 6. Effect of *miR-1297* on the expression of high-mobility group AT-hook 2 (HMGA2) in HepG2 and SMMC7721. (A) Overexpression of *miR-1297* inhibited HMGA2 expression at the protein level. The expression level of the HMGA2 protein in HepG2 and SMMC7721 cells transfected with exogenous *miR-1297* or its inhibitor was analyzed by western blot analysis. β-actin was used as an internal control. (B) Overexpression of *miR-1297* did not significantly affect the *HMGA2* mRNA level in the HepG2 and SMMC7721 cells. The mRNA levels of the *HMGA2* were normalized to β-actin. Data are expressed as mean ± standard error of the mean. N=3. *P<0.05 vs. control; $^{\#}$P<0.05 vs. *miR-1297*.

cells. This finding indicates that *miR-1297* inhibits HMGA2 protein expression in hepatocellular carcinoma.

Discussion

In the present study, *miR-1297* inhibited the proliferation and migration, and promoted the apoptosis of hepatocellular carcinoma, and the direct target of *miR-1297* is the *HMGA2* gene. This finding provides a new therapeutic approach for liver cancer.

Hepatocellular carcinoma is the most common type of liver cancer, accounting for ~90% liver cancers (19). Currently, hepatocellular carcinoma has become the third leading cause of cancer fatalities worldwide (19). Numerous studies have revealed that liver cirrhosis and viral hepatitis infection are two important risk factors of hepatocellular carcinoma (20). In addition, inflammation, necrosis, fibrosis and ongoing regeneration also contribute to cirrhotic liver and lead to the development of hepatocellular carcinoma (2). Recent studies have characterized the altered molecular pathways, such as

p53, PIKCA and β-catenin genes during carcinogenesis, and the mutations on these genes was most frequently reported in patients with hepatocellular carcinoma (21-24). The abnormal activation of Wnt/β-catenin appears to be frequently altered in hepatocellular carcinoma (23,24). mTOR signaling was also shown to have a critical role in the pathogenesis of hepatocellular carcinoma (5). Androgen receptor has been reported to regulate cell adhesion and migration of hepatocellular carcinoma via regulating the β1-integrin-AKT signaling pathway (3). Recently, miRNAs have been recognized as a potential therapeutic target for hepatocellular carcinoma. In the present study, the molecular mechanism of antitumor activity of *miR-1297* on hepatocellular carcinoma was explored.

To investigate whether *miR-1297* has an antitumor role in HepG2 and SMMC7721, the MTT assay was employed to observe the effects of *miR-1297* on cellular viability of HepG2 and SMMC7721. The results showed that *miR-1297* can significantly inhibit the proliferation of HepG2 and SMMC7721 cells, and co-transfection with AMO-1297 can abolish the inhibition of cell viability in HepG2 and SMMC7721 cells. Additionally, the effects of *miR-1297* overexpression were assessed on the apoptosis of HepG2 and SMMC7721, and the results showed that forced expression of *miR-1297* may lead to the apoptosis of HepG2 and SMMC7721. In agreement with the present findings, previous studies also reported that *miR-1297* inhibited the growth of human lung adenocarcinoma cell and colorectal cancer (17,18). COX2 and TRIB2 were identified as the target genes of miR-1297 in two types of cells, and have been shown to be associated with the inhibition of proliferation. However, whether COX2 and TRIB2 are involved in the miR-1297 inhibition of liver cancer cell proliferation remains unknown. It has been reported that TRIB2 contributes to the inhibition of proliferation and the induction of apoptosis of HepG2 cells (25). It is thus proposed that TRIB2 is a possible target of miR-1297 in hepatocellualr carcinoma cells.

Migration of cancer cells is an important factor for cancer metastasis. Inhibition of migration contributed to the treatment of hepatocellular carcinoma (3). The impact of *miR-1297* overexpression on the migration of hepatocellular carcinoma was also observed in the present study. Overexpression of *miR-1297* significantly inhibited the migration of HepG2 and SMMC7721 cells, and co-transfection with AMO-1297 may attenuate the slowed migration of hepatocellular carcinoma by *miR-1297*. Consistently, it has been reported that *miR-1297* inhibited the migration and invasion of human colorectal cancer *in vivo* and *in vitro* (17).

Bioinformatics predication on a microRNA database (TargetScan) was used to screen the possible candidate gene of *miR-1297*. A binding site of *miR-1297* was identified in the 3'UTR of *HMGA2*, suggesting *HMGA2* as a potential target of *miR-1297*. Activation of the *HMGA2* gene was observed in the cells of numerous human malignancies, such as breast cancer, lung cancer and pancreatic carcinoma (26-30). The inhibition or silencing of *HMGA2* contributed to the inhibition of tumor growth, the induction of apoptosis and the suppression of tumor metastasis (31). In the present study, the luciferase assay showed that *miR-1297* overexpression markedly inhibited the luciferase activity of the reporter plasmid harboring the 3'UTR of *HMGA2* gene. To the best of our knowledge, this is the first study to uncover the inhibition effects of *miR-1297* on *HMGA2* in hepatocellular carcinoma cells.

To further confirm that *miR-1297* overexpression inhibits the translation of *HMGA2* in hepatocellular carcinoma, the effects of *miR-1297* were studied on the expression of the HMGA2 protein in HepG2 and SMMC7721. Overexpression of *miR-1297* also reduced the expression of HMGA2 protein in the HepG2 and SMMC7721 cells. Whereas, the mRNA level of *HMGA2* was not affected by overexpression of *miR-1297*. These results suggest that *miR-1297* directly acts on the 3'UTR of *HMGA2* gene.

In conclusion, this is the first study to show that *miR-1297* inhibited the proliferation and migration, and promoted the apoptosis of hepatocellular carcinoma cells via directly targeting the *HMGA2* gene. *miR-1297* is a potential therapeutic target of hepatocellular carcinoma.

Acknowledgements

The present study was supported by the National Natural Science Foundation of China (grant no. 81100483), and the Foundation of Building Key Department of Heilongjiang Province Universities.

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