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Original Article

The Effect of Sirna Interference on CDC14A Expression in the Gastric Cancer Cell Line MNK-45

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Abstract:
Gastric cancer is a malignant tumor that seriously threatens the health of the nation as a whole. However, there is still a lack of precise treatment for advanced and metastatic cancer patients who cannot undergo surgery. Currently, tumor molecular targeted biological therapy has shown potential in the treatment of advanced gastric cancer. The cell cycle 14A (CDC14A) phosphatase is a dual specific phosphatase that widely regulates cell division in eukaryotes. CDC14A can inhibit cell division by mediating the G2/M phase transition, and dysregulation of CDC14A expression plays a role in carcinogenesis. Studies have shown that CDC14A may affect the development of highly microsatellite unstable (MSI-H) gastric cancer by deactivating phosphatase function, but the mechanism by which abnormal expression of CDC14A affects gastric cancer development is not yet clear. Therefore, we investigated the effect of CDC14A on gastric cancer cells by upregulating and knocking down the expression of CDC14A via siRNA. The results revealed that downregulation of CDC14A expression promoted cell entry into the G1 phase, inhibited cell proliferation and in vitro colony formation, whereas upregulation of CDC14A expression promoted cell colony formation. This study preliminarily confirms that CDC14A affects the development of gastric cancer by interfering with cell division and proliferation, laying the foundation for further revealing the mechanism of action of CDC14A in gastric cancer and providing new strategies for molecular targeted biological therapy of gastric cancer.

Keywords: CDC14A, gastric cancer, siRNA, tumor molecular targeted therapy

Introduction

The latest global cancer statistics released by the International Agency for Research on Cancer in 2024 show that gastric cancer is the fifth most common malignant cancer worldwide, accounting for approximately 4.9% of all cancer cases [1-3]. More than 80% of gastric cancer cases are diagnosed in advanced stages, while the 5-year survival rate of gastric cancer patients in China is only 35%, seriously endangering the health of residents [4-6]. Gastric cancer is highly heterogeneous and has a poor prognosis. Although improved radiotherapy, chemotherapy, and surgical treatments are effective, the prognosis of

patients is poor [1,3]. In addition, for patients with unresectable advanced or metastatic tumors, in addition to chemotherapy, only trastuzumab and some immune checkpoint inhibitors, such as nivolumab and pembrolizumab, have shown certain therapeutic effects in HER-2-positive and PD-L1-positive tumor patients, respectively. However, owing to the low overall response rate to immunotherapy and the high degree of heterogeneity among patients, not only is precise screening of immune-dominant populations needed but also accurate, comprehensive, and dynamic evaluation of the immune microenvironment is needed [7-10]. Recently, studies have shown that biological therapies targeting tumor suppressor genes or tumor suppressor genes and related signaling pathways can achieve antitumor effects by acting on specific cell receptors, signaling pathways, angiogenesis, and cell cycle regulation that promote tumor growth, thereby inhibiting tumor cell growth or promoting apoptosis [10-13]. Moreover, compared with traditional cell chemotherapy, tumor molecular targeted biological therapy has strong specificity and minimal toxicity [1, 10, 14]. However, targeted molecular biological therapy for gastric cancer treatment is still in its infancy, and further exploration of gastric cancer treatment is needed.

CDC14A is a highly conserved dual-specificity phosphatase that is widely expressed in eukaryotic organisms and is involved in various biological activities, such as meiosis, cytoplasmic division, mitosis, DNA damage repair, tumor development, and reproductive reproduction [15-18]. Abnormal expression of CDC14A can disrupt the structure of the spindle, affecting chromosome segregation and cytoplasmic division. The overexpression of CDC14A can disrupt the structure of chromosomes and inhibit the regeneration and growth of microtubules, leading to abnormal spindle morphology. It plays an important role in the function of the spindle and various steps of mitosis [19, 20]. Studies have shown that abnormal expression of CDC14A can lead to chromosomal segregation [21, 22], whereas normal operation of the cell cycle is the result of the orderly expression and regulation of cell cycle proteins in time and space. Cells that cannot complete the normal cell cycle undergo apoptosis or carcinogenesis. In addition, Clemente Blanco et al. reported that CDC14A can promote telomere separation by inhibiting the transfer of RNA polymerase II, leading to telomere abnormalities and ultimately causing cellular carcinogenesis [23]. These findings indicate that abnormal expression of CDC14A can lead to cellular genomic instability, thus playing an important role in the development of tumors.

Studies have shown that CDC14A is differentially expressed in human cancer cell lines and can increase the expression of the CDC14A phosphatase by blocking DNA methylation, histone deacetylation, or proteasome activity. However, in most tumor cell lines with high expression of the tumor suppressor gene p53, the expression level is lower [24, 25]. Under normal circumstances, p53 is an important tumor suppressor gene that inhibits the growth of tumor cells while also suppressing tumorigenesis in the body, thereby affecting cell proliferation and suppressing tumor development [26]; however, when its function is lost, it may lead to infinite cell proliferation, ultimately resulting in cell apoptosis or carcinogenesis. Studies have shown that CDC14A can interact with p53 both in vitro and in vivo and specifically dephosphorylates the ser315 site of p53 in vitro [15, 24, 27]. This site can be phosphorylated by Cdk2/cyclin A and Cdk1/cyclin B in vitro and by cyclin A in cells, indicating that the CDC14A phosphatase may act as an antagonist of Cdk and cyclin, thereby participating in tumor growth and development [24]. An analysis of single nucleotide repeat sequence mutations in microsatellite-unstable gastric cancer revealed that 6% of gastric cancer patients had mutations in the CDC14A gene, but only in highly microsatellite-unstable (MSI-H) gastric cancer patients. Moreover, CDC14A mutations may play a role in the development of highly microsatellite unstable (MSI-H) gastric cancer by disrupting the function of phosphorylases during cell signaling [28].

In this study, we used siRNAs to upregulate and knockdown the expression of CDC14A to investigate its effect on gastric cancer. Through in vitro cell cycle analysis, we found that downregulation of CDC14A expression promotes cell entry into the G2/M phase, thereby promoting cell division. The overexpression of CDC14A inhibits normal cell division. In addition, through cell proliferation and colony formation experiments, we found that downregulating the

expression of CDC14A reduces the proliferation and in vitro colony formation ability of MKN-45 cells, whereas the overexpression of the CDC14A phosphatase enhances the proliferation and in vitro colony formation ability of these cells. We preliminarily confirmed that CDC14A affects the development of gastric cancer by interfering with cell division and proliferation. These findings lay the foundation for further revealing how the CDC14A phosphatase is involved in the pathogenesis and progression of gastric cancer and suggest new ideas for molecular targeted therapy of gastric cancer in clinical practice.

2. Materials and methods

2.1 Method

2.2.1 Construction of small interfering RNA sequences that overexpress and downregulate CDC14A for transfection into the gastric cancer cell line MKN-45

MKN-45 (CL-0292, Pricella, Wuhan, China) suspensions at a density of 1×10^6/mL were inoculated into cell culture plates, and the degree of fusion was approximately 90%. The miRNA plasmid containing the meaningless gene SI-CDC14A-nc, downregulated genes SI-CDC14A-1, SI-CDC14A-2, and SI-CDC14A-3, and the pcDNA3.1 plasmid containing the upregulated gene SI-CDC14A-OE were transfected into MNK-45 cells via Lipofectamine® 2000 Reagent (11668-019, Invitrogen, USA) according to the instructions. The above groups were divided into MKN-45-nc, MKN-45-SI-CDC14A-1, MKN-45-SI-CDC14A-2, MKN-45-SI-CDC14A-3, and MKN-45-CDC14A-oe groups. Untransfected MKN-45 cells were used as the control group.

Table 1 Primers for quantitative real-time PCR

RNA/DNA	sequence (5'-3')
SI-CDC14A-1	AGUAGUUCUCUGUAUUAAAGG
SI-CDC14A-2	GGUUAAUGACUACUAUAAAUG
SI-CDC14A-3	GUCUAUUGGUGGAAAUCUUUC
SI-CDC14A-nc	UUCUCCGAACGUGUCACGUTT
CDC14A-oe	a tggcagcgga gtcaggggaa ctaatcgggg cttgtgagtt catgaaagat cggttatatt ttgctacttt aaggaataga ccaaaaagca cagtaaatac ccactatttc tccatcgatg aggagctggt ctatgaaaat ttctatgcag attttggacc gctgaacttg gcaatggtgt acagatattg ctgcaaacta aacaagaaac taaaatcata cagtttgtca agaaagaaaa tagtgcacta cacctgtttt gaccaacgga aaagagcaaa tgcagcattt ttgataggtg cctatgcagt aatctattta aagaagacac cagaagaagc ctacagagca ctcctgtctg gctcaaaccc cccctatctt ccattcaggg atgcttcctt tggaaattgc acttacaatc tcaccattct cgactgtttg cagggaatca gaaagggatt acaacatgga ttttttgact ttgagacatt tgatgtggat gaatatgaac attatgagcg agttgaaaat ggtgacttca actggattgt tccaggaaaa tttttagcat ttagtggacc acatcctaaa agcaaaattg agaatggtta tcctcttcac gcccctgaag cctactttcc ttatttcaaa aagcataatg tgactgcagt tgtgaggcta aacaaaaaga tttatgaggc aaagcgcttc acagacgctg gcttcgagca ctatgacctc ttcttcatag atggcagcac acccagtgac aacatcgtgc gaaggttcct gaacatctgt gagaacaccg aaggggccat cgccgttcac tgcaaagctg gtcttggaag aacagggaca ttgatagcct gttatgtaat gaaacactac aggtttacac atgctgaaat aattgcttgg attagaatat gccggccagg ctctattata ggaccccagc agcacttcct ggaagaaaaa caagcatcgt tgtgggtcca aggagacatt ttccgatcca aactgaaaaa tcgaccatcc agtgaaggaa gtattaataa aattctttct ggcctagatg atatgtctat tggtggaaat ctttcaaaaa cacaaaacat ggaacgattt ggagaggata acttagaaga tgatgatgtg gaaatgaaaa atggtataac ccagggagac aaactacgtg ccttaaaaag tcagagacag ccacgtacct caccatcctg tgcatttagg tcagatgata caaaaggaca tccaagagca gtgtcccagc ctttcagatt aagttcatcc ctgcaaggat ctgcagttac tttgaagaca tcaaaaatgg cactgtcccc ttcagcaacg gccaagagga tcaacagaac ttctttgtct tcgggtgcca ctgtaagaag cttttccata aactcccggc tagccagttc tctagggaac ttgaatgctg caacagatga tccagagaac aaaaagacct cctcatcctc taaggcaggc ttcacagcca

gcccgtttac caacctcttg aatggcagct cccagccaac taccagaaat taccctgagc
tcaacaataa tcagtacaac agaagcagca acagcaacgg gggcaacctg aacagccccc
caggccccca cagcgccaag acagaggagc acaccaccat cctccgaccc tcctacaccg
ggctttcttc ttcttcagcg agattcctga gccgttctat cccttgttca tgcctactgc
tagtctttag gaagcccttt cttggaagcc ccctgctctc cttaccaatt tctcatctttaa

2.2.2 qRT–PCR Detection of CDC14A mRNA Expression

qRT–PCR was used to measure the expression of CDC14A mRNA in each group of MKN-45 cells. Redzol (FTR-50, SBS, Beijing, China) was added to extract total RNA from the six groups of cells. The purity and concentration of the extracted RNA were measured via a spectrophotometer. On the basis of the detection results, DEPC water was used to adjust the concentration of each group of samples to an appropriate level. A cDNA reverse transcription kit (QP056, GeneCopeia, USA) was used to reverse transcribe the total RNA into cDNA. β-actin was used as an internal reference gene, and cDNA was used for qRT–PCR detection of CDC14A expression. The primers used for quantitative real-time PCR are listed in Table 2. The reaction conditions were as follows: predenaturation at 95°C for 10 min, 95°C for 15 s, and 60°C for 1 min. A total of 40 cycles were completed, with 3 replicates set up for each sample. The primer sequence was synthesized by Shanghai Bioengineering Co., Ltd. The relative β-actin expression level of CDC14A was calculated via the $2^{-\Delta\Delta Ct}$ method.

Primer Sequences:

Table 2 Primers for quantitative real-time PCR

Gene	Forward sequence (5’-3’)	Reverse sequence (3’-5’)
CDC14A	TACAAAAGGACATCCAAGAGCAG	TGGCACCCGAAGACAAAGA
β-actin	AGATCAAGATCATTGCTCCTCCTG	CATTTGCGGTGGACGATGGA

2.2.3 Detection of CDC14A Protein Expression Via Protein Immunoblotting

Proteins were extracted from the six groups of cells via RIPA lysis buffer (BN25001, Bairui Ji, Beijing, China), and the protein concentration was determined via a BCA assay kit (SL201, UteBody, Tianjin, China). First, the denatured protein was added to the buffer mixture. Then, 10% SDS–PAGE (AR1146-10, PhD, Wuhan, China) with 50 μg of protein per lane was performed to separate the proteins. The proteins were transferred onto a PVDF membrane, which was subsequently blocked with 5% skim milk powder at 37°C for 2 hours. The CDC14A primary antibody (34-8100, Abcam, Cambridge, UK) and β-actin (internal reference) primary antibody (ab8227, Abcam, Cambridge, UK) (1:500, 1:2500) were added, and the samples were incubated overnight at 4°C. After the membranes were washed with TBST three times, they were incubated with a horseradish peroxidase-labeled secondary antibody (ab205718; Abcam, Cambridge, UK) at room temperature for 1 hour. The samples were washed with TBST three times for 10 minutes each. ECL liquid darkroom luminescence development was performed, and after image acquisition, density analysis of the imprint was performed via ImageJ software (Media Cybernetics, Silver Spring, MD, USA).

2.2.4 Flow Cytometry Detection of the Cell Cycle

A total of 10^6 cells were cultivated in a 6-well plate, cultured overnight and restored to a normal state. Then, the cells from each group were digested with 0.25% trypsin, 2×10^5–10^6 resuspended cells were removed, the mixture was centrifuged at 1000 rpm for 5 minutes, the supernatant was discarded, and the mixture was fixed overnight with precooled 75% ethanol. The samples were washed once with PBS and centrifuged, and the supernatant was discarded. One milliliter of DNA Staining Solution was added, and the mixture was vortexed for 10 s to mix well. The mixture was incubated at room temperature in the dark for 30 minutes. The lowest sample loading speed was selected, and detection was performed on a flow cytometer.

2.2.5 Cell Cloning Experimental Report

The cells whose wall adhesion rate was >80% (in

the logarithmic growth phase) were removed, digested and centrifuged, and the cells were resuspended and counted. A 12-well plate was seeded, with approximately 500 cells added to each well, and the cells were cultured in a CO_2 incubator. Conventional cultivation lasts for 14 days, during which the culture medium is changed according to the cell state. The culture medium was discarded, and the samples were gently washed twice with PBS. One milliliter of cell fixative was added to a 12-well plate and fixed for 30 minutes. The cell fixative was discarded, the samples were gently washed twice with PBS, and 1 mL of 0.1% crystal violet (G1062, Solarbio, Beijing, China) was added for 3 minutes of staining. The crystal violet solution was discarded, the samples were washed with PBS until the bottom of the well plate was clear, and then the samples were photographed for counting.

2.2.6 CCK8 Experiment

According to the instructions of the CCK-8 detection kit (C0039, Beyotime, Shanghai, China), cells in the logarithmic growth phase were seeded into a 96-well plate, with 3 wells set up. The culture medium was added, and the cells were cultured in a 37°C incubator for 24, 48, or 72 hours. The cells were washed three times with PBS at different time points, 10 μL of CCK8 solution was added to each well, the mixture was incubated at 37°C for 2 hours, and the OD value of each well was measured at a wavelength of 450 nm via an enzyme analyzer.

2.2 Data Processing

GraphPad 8.0.1 was used for data processing, and one-way analysis of variance was used for intergroup comparisons. $P<0.05$ indicated statistically significant differences.

3. Results

3.1 Expression Levels of CDC14A Mrna and Protein after Sirna Transfection into MNK-45 Cells

By using the meaningless gene SI-CDC14A-nc, the downregulated genes SI-CDC14A-1, SI-CDC14A-2, and SI-CDC14A-3 and the upregulated gene SI-CDC14A-oe were transfected into MNK-45, resulting in MKN-45-nc, the CDC14A-knockdown group MKN-45-SI-CDC14A-1, MKN-45-SI-CDC14A-2, the MKN-45-SI-CDC14A-3, and the CDC14A-upregulated group MKN-45-CDC14A-oe. RT–PCR was used to detect the expression of CDC14A in each group, and the results (Figure 1A) revealed that there was no difference between the MKN-45 nc group and the MKN-45 group, confirming that the interference experimental steps modified with meaningless RNA sequences had no effect on this experiment. Compared with those of the downregulated genes MKN-45-SI-CDC14A-1, MKN-45-SI-CDC14A-2, MKN-45-SI-CDC14A-3, the expression of CDC14A was significantly lower in MKN-45-SI-CDC14A-2 ($P<0.01$), indicating that MKN-45-SI-CDC14A-2 has the best interference efficiency. In addition to the overexpression gene MKN-45-CDC14A-oe, the expression level of CDC14A in the MKN-45-nc group was significantly greater than that in the MKN-45-CDC14A-oe group ($P<0.01$), whereas there was no difference between the MKN-45 group and the MKN-45-nc group. Owing to the optimal interference efficiency of MKN-45-SI-CDC14A-2 cells, we used MKN-45-CDC14A-2 cells for interference in subsequent experiments.

According to the WB results (Figure 1B), the expression level of CDC14A was significantly lower in the MKN-45-nc group than in the MKN-45-CDC14A-2 group ($P<0.01$), confirming that the downregulation of the MKN-45-CDC14A-2 gene resulted in a decrease in CDC14A phosphatase expression in MKN-45 cells. Compared with that in the MKN-45-CDC14A-oe group, the expression level of CDC14A in the MKN-45-nc group was significantly greater ($P<0.05$), confirming that the protein level of the CDC14A phosphatase increased in gastric cancer cells overexpressing CDC14A.

3.2 Flow Cytometry Detection of the Cell Cycle

Flow cytometry was used to detect the cell cycle distribution of the MKN-45, MKN-45-nc, MKN-45-SI-CDC14A, and MKN-45-CDC14A-oe groups (Figure 2). The results revealed that all four groups presented different stages of the cell cycle. Compared with that in the G0/G1 phase, the number of cells in the S phase decreased, and the number of cells in the G2/M phase decreased compared with that in the S phase, which confirmed the orderly progression of the cell cycle. The results also revealed that in the MKN-45-SI-CDC14A-2 group, compared with that in the MKN-45-nc group, the number of cells in the G0/G1 phase was significantly greater ($P<0.01$),

whereas there was no significant change in the number of cells in the S phase, and the number of cells in the G2/M phase was significantly lower (P<0.01). Compared with the MKN-45-nc group, the MKN-45-CDC14A-oe group presented a significant decrease in the number of cells in the G0/G1 phase (P<0.05), an increase in the number of cells in the S phase (P<0.05), and no significant changes in the number of cells in the G2/M phase. The results showed that downregulation of CDC14A expression promoted the entry of MKN-45 cells into the G0/G1 phase and inhibited cell division.

3.3 Cell Colony Formation Experiment

Cell colony formation experiments were used to observe the growth of the colony-forming cells in each group. After the cells were stained with 0.1% crystal violet (Figure 3), the growth of the colony-forming cells in the MKN-45-SI-CDC14A group was significantly lower than that in the MKN-45 and MKN-45-nc groups (P<0.01). A comparison of the proliferation of colony-forming medium from MKN-45-CDC14A-overexpressing cells with that of control MKN-45 and MKN-45-nc cells revealed that the number of colony-forming media enriched with CDC14A phosphatase significantly increased, and satellite phenomena were observed (P<0.01). The results showed that downregulation of CDC14A expression inhibited the growth and proliferation of colony-forming cells.

3.4 CCK8 Experiment

There was no significant change in cell proliferation in the control groups (MKN-45 and MKN-45-nc) after 24, 48, and 72 hours of culture in a 37°C incubator (Figure 4). Compared with that in 24 h, the proliferation of the gastric cancer cells with downregulated MKN-45-SI-CDC14A gene expression tended to decrease at 48 and 72 h after culture (P<0.01). The proliferation of gastric cancer cells overexpressing MKN-45-CDC14A tended to increase at 48 and 72 hours after culture compared with 24 hours (P<0.01).

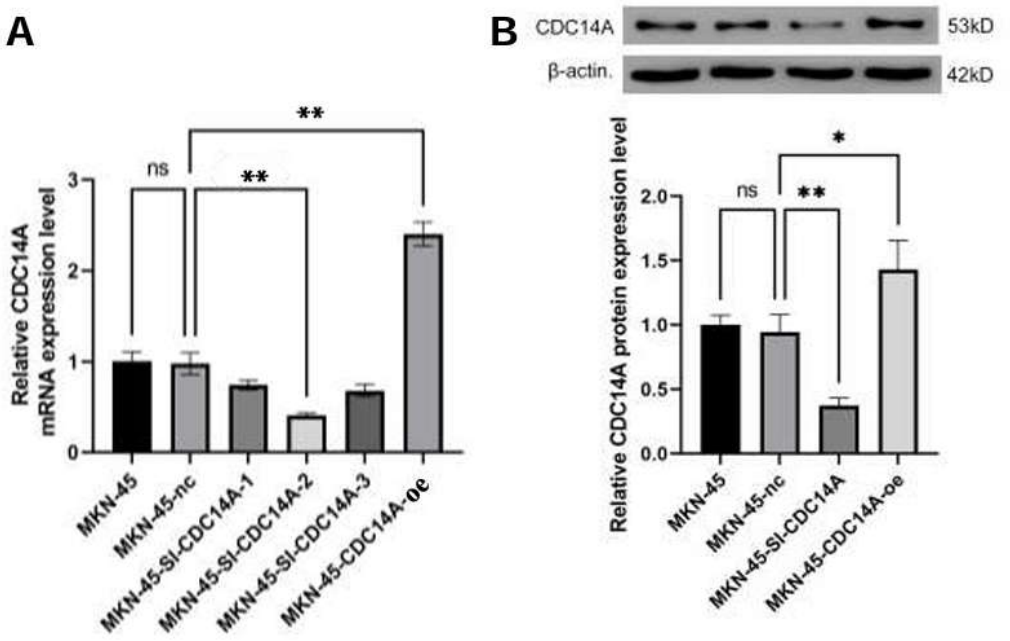

Figure 1 CDC14A mRNA and protein expression levels after siRNA transfection into MNK-45. A. After siRNA transfection into MNK-45, the expression of CDC14A mRNA in each group of cells showed no significant difference, with ns indicating no significant difference. B. After siRNA transfection into MNK-45, the expression of CDC14A protein in each group of cells showed no significant difference, with ns indicating no significant difference. * indicating P<0.05, and ** indicating P<0.01.

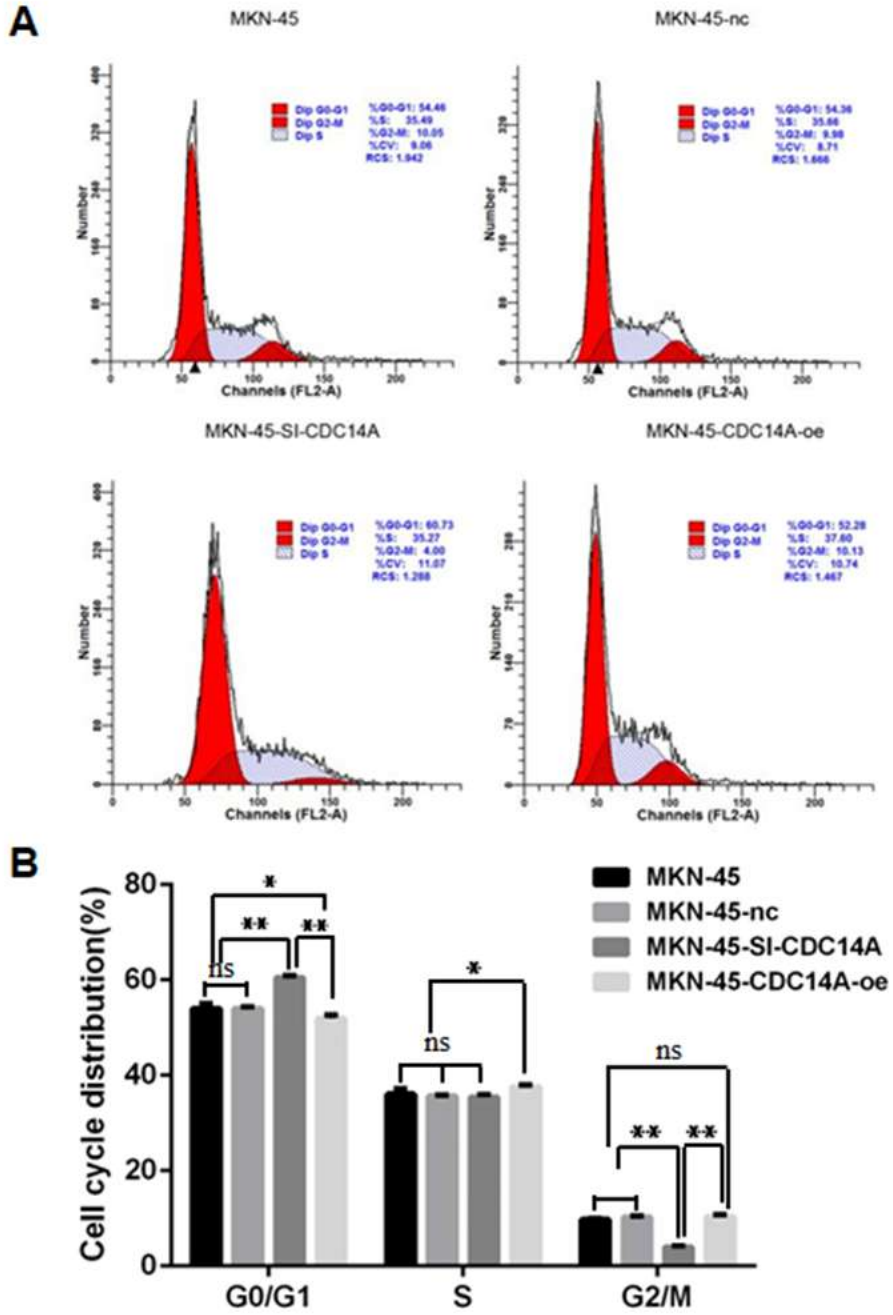

Figure 2 Cell cycle changes after siRNA transfection of MNK-45. A. Flow cytometry was used to detect the cell cycle of each group after siRNA transfection into MNK-45. B. The changes in G0/G1, S, and G2/M phases of cells in each group after siRNA transfection of MNK-45. Ns represents no significant difference, * represents P<0.05, ** represents P<0.01.

4. Discussion

Gastric cancer is the fifth most commonly diagnosed cancer and the fourth leading cause of cancer death worldwide. Owing to the insidious early symptoms and advanced stage of diagnosis, as well as the high heterogeneity among gastric cancer patients, precise treatment is currently lacking [2,3]. The emergence of targeted therapy for tumor molecules has opened a new era in the treatment of gastric cancer through the inhibition of tumor genes or the promotion of tumor suppressor genes and their related signaling pathways to suppress tumor development [6, 29]. CDC14A is a phosphatase closely related to the cell cycle. Previous studies have shown that CDC14A may interfere with the development of gastric cancer by affecting the function of the tumor suppressor gene p53 [24]. We preliminarily confirmed through in vitro experiments that downregulating CDC14A promotes MKN-45

division and inhibits cell proliferation and colony formation. CDC14A may play a role in regulating the cell cycle and cloning ability of cancer cells. Owing to its ability to affect both the cell cycle and tumor suppressor genes, CDC14A has shown great potential in molecular targeted therapy for gastric cancer.

The normal cell cycle plays a decisive role in maintaining normal cell function. Studies by María D V-N and Vázquez-Novelle MD et al. on human cells [22,30] have shown that downregulation of CDC14A expression accelerates cell transition through the G2/M transition phase; CDC14A not only increases its expression level during the G2/M transition but also further enhances its catalytic activity. It can directly bind to Cdc25B and phosphorylate Cdc2 kinase in the N-terminal domain of Cdc25B, causing it to dephosphorylate and inhibit its catalytic activity. Furthermore, it inhibits the activity of Cdc2 kinase, blocking cell division in the G2 phase, indicating that the CDC14A phosphatase promotes the G2/M transition of the cell cycle by regulating the activity of Cdc25B [30-32]. The results of the flow cytometry cell cycle assay in this study also revealed that the number of gastric cancer cells in the downregulated CDC14A phosphatase group was greater in the G0/G1 phase and that there was no significant change in the S phase compared with that in the control group; however, there was a significant decrease in the number of cells in the G2/M phase, confirming that downregulating CDC14A expression can lead to entry into the G2/M phase of the cell cycle and promote cell division. Compared with the control cells, the gastric cancer cells overexpressing CDC14A phosphatase presented a decrease in the number of cells in the G0/G1 phase and an increase in the number of cells in the S phase, with no significant changes in the number of cells in the G2/M phase; these findings confirmed that cell cycle arrest and the inability to complete normal cell division occurred. The results of the cell colony formation experiments and CCK8 experiments revealed that interference with high and low expression levels in MKN-45 cells also led to corresponding changes in the proliferation ability of gastric cancer cells: downregulating CDC14A expression resulted in a decrease in the proliferation ability of gastric cancer tumor cells. In contrast, CDC14A overexpression increased the proliferation ability of gastric cancer cells, further confirming the conclusion that CDC14A phosphatase can affect the malignancy of tumors.

The invasiveness and metastatic potential of tumor cells are highly important for evaluating the malignancy of tumors and formulating treatment plans. In this study, a colony formation assay revealed that the number of colonies enriched with downregulated CDC14A expression was significantly lower than that enriched with upregulated CDC14A expression, indicating that downregulating CDC14A reduces the invasion and metastasis ability of gastric cancer cells and inhibits tumorigenesis in vivo. Studies have shown that CDC14A colocalizes with F-actin at the forefront of cells and stress fibers to regulate actin dynamics [33,34], and the antagonistic activity of ERK and hCDC14A against conserved phosphorylation sites on eplin maintains the balance of eplin phosphorylation, thereby regulating actin dynamics to regulate the migration and adhesion of normal and transformed cells. CDC14A dephosphorylates eplin to reduce actin dynamics and limit tumor malignancy [35,36]. Therefore, hCDC14A is also an important factor in inhibiting tumor invasiveness.

Through the above research, we confirmed that CDC14A interferes with the occurrence and development of gastric cancer by affecting the cell cycle, proliferation ability, invasiveness, and tumorigenicity of gastric cancer cells. In the future, we will use mass spectrometry and bioinformatics analysis in proteomics (such as protein–protein interaction (PPI) network analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis) to identify differentially expressed proteins (DEPs) and analyze related signaling pathways to further determine the mechanism and site of the impact of the CDC14A phosphatase on the cell cycle progression of gastric cancer cells, providing good news for the treatment of advanced gastric cancer.

Conclusion

CDC14A may serve as a target for molecular targeted therapy of gastric cancer, thereby inhibiting its development. This study lays a solid foundation for promoting molecular targeted therapy for patients with gastric cancer, helping to develop the best personalized treatment strategies

and improving the overall survival rate and quality of life of patients.

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Author contributions **Guga Suri & Xiaofang Wang:** Methodology, Formal analysis, Investigation, Results, Data curation, Writing-original draft. **Rong Guo, Huiying Cong & Weixin Li:** Validation, Resources, Writing-original draft. **Guoying Fan & Jiale Wei:** Methodology, Resources, **Tianwei Yu:** Conceptualization, Methodology, Validation, Data Curation, Resources, Writing-original draft.

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Data availability No datasets were generated or analyzed during the current study.

Declarations

Competing interests The authors declare that they have no competing interests.

Ethical approval Not applicable.

Consent to participate Not applicable.

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