

## Original Article

# LINC00630 as a miR-409-3p sponge promotes apoptosis and glycolysis of colon carcinoma cells via regulating HK2

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**Abstract:** Long-chain non-coding RNAs (lncRNAs) belong to the family of non-coding RNAs and contain more than 200 nucleotides. They are involved in the growth, apoptosis, and glycolysis of carcinoma cells. A newly discovered lncRNA, LINC00630, has been reported in colon carcinoma. In this study, we found that the expression of LINC00630 was remarkably upregulated in colon carcinoma tissues and cell lines compared with that in adjacent tissues and the NCM-460 cell lines. Knocking out LINC00630 resulted in inhibition of proliferation and glycolysis but increase in apoptosis. In addition, we confirmed the direct interaction between LINC00630 and miR-409-3p in colon carcinoma cells using bioinformatics methods and dual luciferase reporter gene assay. Finally, we demonstrated that LINC00630 could promote cell growth and glycolysis and inhibit apoptosis by functioning as a miR-409-3p sponge, and further regulate hexokinase 2 (HK2) in colon carcinoma cells. Our results confirmed that LINC00630 regulates proliferation, glycolysis, and apoptosis mainly through targeting the miR-409-3p/HK2 axis, which may explain the progression of colon carcinoma and provide a potential target for the treatment of colon carcinoma.

**Keywords:** LINC00630, miR-409-3p, HK2, colon carcinoma, glycolysis

## Introduction

Colon carcinoma is a disease with poor prognosis and high mortality, and is one of the major causes of carcinoma-related death worldwide [1]. The incidence of colon carcinoma is on the rise owing to extensive changes in lifestyle and dietary habits, and according to reports, the age of onset of colon carcinoma tends to be younger in China [2]. Currently, colon carcinoma is considered to be correlated with environmental and genetic factors [3]. A study has shown that the main factors affecting the incidence of colon carcinoma include environment, diet, intestinal homeostasis, alcohol and smoking addiction, and lack of physical exercise [4]. At present, surgery and chemotherapy are the main treatment methods [5]. However, challenges such as late diagnosis, drug resistance, and metastasis are yet to be addressed [6].

Therefore, the present research focused on exploring the markers for early diagnosis and the growth and metastasis of colon carcinoma.

Long-chain non-coding RNAs (lncRNAs) contain 200-100,000 nucleotides, lack an active open reading frame, and are transcribed by RNA polymerase II without any protein coding role [7, 8]. The lncRNAs are involved in the regulation of chromatin modification, transcription interference, transcription activation, nuclear transport, alternative splicing, and protooncogene activation, thereby regulating gene expression at epigenetic, transcriptional, or post-transcriptional levels [9, 10]. Several studies have reported that the abnormal expression and function of lncRNAs are related to the progression of many diseases, especially malignancies [11, 12]. For instance, Chen et al. [13] found that lncRNA PVT1 promoted the progression of gall-

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**Table 1.** The sequence of transfection vectors

Name	Sequence	Company
LINC00630	Chromosome X: 102, 769, 158-102, 885, 406 forward strand GRCh38:CM000685.2	Sangon Biotech (Shanghai) Co., Ltd
miR-409-3p	5iRGAAUGUUGCUCGGUGAACCCCU-3	Sangon Biotech (Shanghai) Co., Ltd
Empty vector plasmid	pcDNA3.1-NC	Addgene, Cambridge, USA
LINC00630, over-expression plasmid	pcDNA3.1-LINC00630	Sangon Biotech (Shanghai) Co., Ltd
si-HK2	5i-ACGACAGCATCATTGTAA-3	Sangon Biotech (Shanghai) Co., Ltd
miR-409-3p simulated NC plasmid	5iRAGGTAGCTGCCTAGAGCAG-3	Sangon Biotech (Shanghai) Co., Ltd
miR-409-3p-mimics	5iR-409-3p-mimics	Sangon Biotech (Shanghai) Co., Ltd

bladder carcinoma by regulating the microRNA (miR)-143/hexokinase 2 (HK2) axis, whereas Zhou et al. [14] found that LncRNA XIRP2-AS1 suggested good prognosis of colon carcinoma.

LINC00630 is a newly discovered lncRNA located on the human Xq22.1 chromosome. An early study has uncovered that LINC00630 is differentially expressed in lung carcinoma and is involved in the occurrence of the disease [15]. However, the mechanism of LINC00630 effect in colon carcinoma remains unclear.

Glycolysis is a representative characteristic of tumors. As proposed by Warburg nearly 90 years ago [16], carcinoma cells rely on glycolytic fermentation to generate energy and thus have no correlation with oxygen tension in the environment [17]. LINC00630 is highly expressed in colon carcinoma cells and can inhibit glycolysis to promote their apoptosis. Therefore, targeting LINC00630 is expected to be a potential strategy for the clinical treatment of colon carcinoma.

## Materials and methods

### Clinical data

We included 45 cases of colon carcinoma patients that underwent treatment from February 2013 to February 2014. Colorectal tumor tissues and the adjacent tissues were collected intraoperatively. Tumor tissues were stored at -80°C. The patients did not receive radiotherapy or chemotherapy prior to surgical intervention. This study was approved by the Ethics Committee of Changzhou Second People's Hospital, The Affiliated Hospital of Nanjing Medical University (No. [2018]KY037-01), and written informed consent was obtained from each patient.

### Cell cultivation

HT-29, SW480, LOVO, HCT116, and NCM-460 were obtained from the American Type Culture Collection and cultivated in RPMI 1640 medium or Dulbecco's modified Eagle's medium supplemented with 10% fetal bovine serum (Invitrogen, California) and 5% CO<sub>2</sub>.

### Cell transfection

The sequences of LINC00630 (Chromosome X: 102, 769, 158-102, 885, 406 forward strand GRCh38: CM000685.2) and miR-409-3p, empty vector plasmid (pcDNA3.1-NC), LINC00630 over-expression plasmid (pcDNA3.1-LINC00630), LINC00630 siRNA negative control plasmid (si-NC), si-LINC00630 plasmid (si-LINC00630), si-HK2, miR-409-3p simulated NC plasmid (NC-mimics), and miR-409-3p-mimics were constructed by Sangon Biotech (Shanghai) Co., Ltd. Twenty-four hours before transfection, the cells were inoculated into 6-well plates. When confluence reached 30-50%, 50 nM siRNA or miRNA was transfected into the cells using Lipofectamine 3000 reagent (Invitrogen). The cells were then cultivated in 5% CO<sub>2</sub> for 6-8 h, and further cultivated in complete medium for 24-48 h. The transfection sequences are shown **Table 1**.

### Quantitative real-time-polymerase chain reaction (qRT-PCR)

For mRNA expression detection, total RNA was extracted with TRIzol Kit (Invitrogen, Carlsbad, CA, USA) and reverse-transcribed into cDNA with M-MLV reverse transcriptase (Promega, Madison, WI, USA). QRT-PCR was performed using the SYBR ExScript RT-qPCR Kit (Takara, Dalian, China) in ABI 7500 Real-Time PCR system (Applied Biosystems; Thermo Fisher Scientific, Inc.) with U6 as endogenous control,

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**Table 2.** Primer sequence

Gene	Upstream (5'-3')	Downstream (5'-3')
LINC00630	TAACCCAGTGCCTCGTATGGT	GCATGAAGAGTTGCACAGGGA
miR-409-3p	GGCTCTGGCTCCGTGTCTT	CAGTGCAGGGTCCGAGGTATT
HK2	AACAGCCTGGACGAGAGCATC	AGGTCAAACCTCTCGCCG
U6	CAAATTCGTGAAGCGTTCATA	AGTGCAGGGTCCGAGGTATTC
GAPDH	CCTGTACGCC AACACAGTGC	ATACTCTGCTTGCTGATCC

and each sample was measured in triplicate. The total volume of the reaction mixture was 20  $\mu$ L, which contained 1  $\mu$ L cDNA, 10  $\mu$ L SYBR Premix EX Taq, 1  $\mu$ L each of the primers (10  $\mu$ M), and 7  $\mu$ L ddH<sub>2</sub>O. The PCR program was as follows: 95°C for 3 min followed by 40 cycles of 95°C for 10 s, and 60°C for 30 s. All fold changes were calculated using the comparative Cq ( $\Delta\Delta$ Cq) method using U6 for normalization [18]. The primer sequences are shown **Table 2**.

### Cell proliferation

Cells ( $1 \times 10^5$  cells/well) were cultivated on a 96-well plate for 24 h. CCK-8 (Beyotime, Shanghai, China) was subsequently utilized for proliferation detection. The cells were then cultivated for another 24, 48 or 72 h, and incubated with 10  $\mu$ L CCK-8 for 4 h. The absorbance in the plate was measured at 450 nm.

### Apoptosis

Cell apoptosis was detected by flow cytometry analysis using FITC-Annexin V/PI Apoptosis Detection kit (BD Pharmingen, San Diego, CA, USA). Cells ( $2 \times 10^5$ ) were inoculated into 6-well plates for 48 h. Then, the cells were rinsed with phosphate-buffered saline, resuspended, and stained. The apoptotic cells were detected using flow cytometry (Beckman, Miami, FL, USA).

### Glucose consumption, lactic acid production, and pyruvate kinase activity

The colon carcinoma cells were collected 24 h after transfection, and glucose consumption, lactic acid production, and pyruvate kinase (PK) activity were measured using assay kits (Hefei Laier Biological Technology Co., Ltd.).

### Western blot (WB)

The transfected cells were lysed on ice with RIPA. A bicinchoninic acid assay (BCA protein assay kit) was utilized to determine the pro-

tein concentration. Subsequently, 30  $\mu$ g of the equivalent amount of protein in each sample was treated with 10% sodium dodecyl sulfate-polyacrylamide gel electrophoresis, transferred to a nitrocellulose membrane, and sealed with 5% skim milk. After washing with Tris-buffered saline and polysorbate

20, the membrane was incubated with primary antibodies against HK2 (ab209847, abcam, 1:1000) and  $\beta$ -actin (ab8226, abcam, 1:1000) and then incubated with goat anti-rabbit second antibody (ab7090, abcam, 1:5000). The protein bands were evaluated.  $\beta$ -actin was used as internal control, and the experiment was repeated three times.

### Dual-Luciferase reporter

LINC00630 cDNA was treated with pmirGLO to form pmirGLO-LINC00630-wt and pmirGLO-LINC00630-reporter, which were co-transfected with miR-409-3p or miR-NC into HEK-293FT cells. After 48 h, dual-luciferase reporter gene detection (Promega) was performed. The verification method for miR-409-3p and HK2 was similar to that used above.

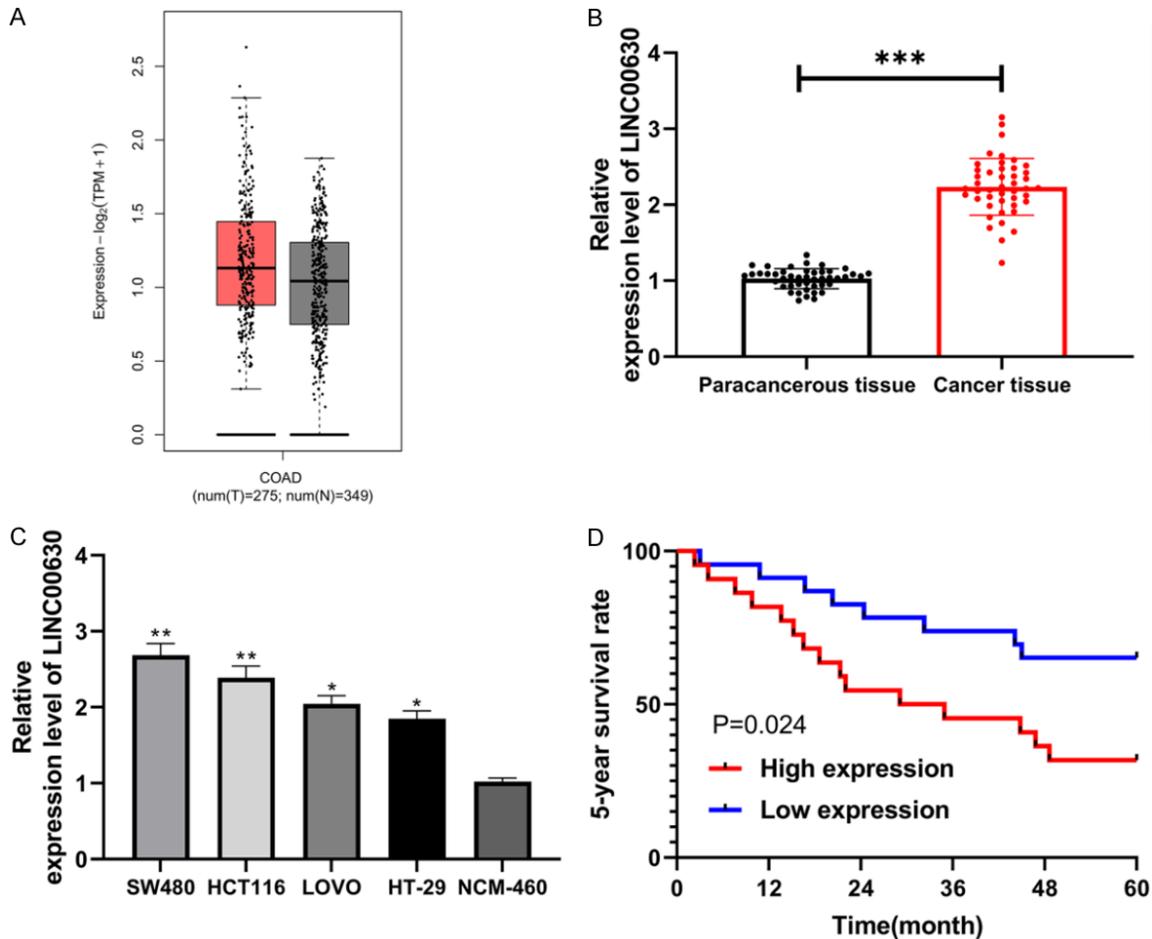
### RIP experiment

Detection was carried out using EZMagna RIP (Millipore). SW480 cells were lysed with RNA immunoprecipitation protocol (RIP). The SW480 cell extract and anti-Argonaute 2 conjugated with magnetic beads or the control anti-IgG antibody were incubated at 4°C for 6 h. Purified RNA was measured using RT-qPCR after removing the globin.

### Growth of transplanted tumor in nude mice

All animal experiments were conducted in accordance with the guidelines established by the Animal Care and Utilization Committee. Ten BALB/c nude mice (Charles River Laboratories, Japan) were reared under specific pathogen-free conditions. SW480 cells treated with sh-LINC00630 or sh-NC were suspended in 200  $\mu$ L of culture medium and injected into nude mice. The tumor size was recorded according to the formula  $v = 1/2 \times ab^2$  (maximum [A] and minimum [B] length of tumor). After 28 days, the mice were sacrificed by cervical dislocation under anesthesia (2.5 mg/100 g body weight pentobarbital injection), and the tumor was removed to measure the weight.

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**Figure 1.** Expression and survival analysis of LINC00630 in colon carcinoma. A. GEPIA2 online analysis of LINC00630 in colon carcinoma in the TCGA database. Tumor n=275, normal n=349. B. qRT-PCR was utilized to assess LINC00630 in tumor tissues of patients with colon carcinoma. n=45. C. Detection of LINC00630 in colon carcinoma cell lines using qRT-PCR. n=3. D. K-M survival analysis of the correlation of LINC00630 with the survival of colon carcinoma patients. n=45. \*indicates  $P < 0.05$ ; \*\*indicates  $P < 0.01$ ; \*\*\*indicates  $P < 0.001$ .

## Statistical analysis

GraphPad 8 was applied for data processing. Data distribution was measured using the Kolmogorov-Smirnov test. Normally distributed data were represented as mean  $\pm$  standard deviation. An independent sample t-test was applied for pair-wise comparison. Count data were represented as percentage (%), and Chi-square test was applied for the comparison. One-way analysis of variance followed with Bonferroni post hoc test was used for multi-group comparison or comparison at multiple time points. Pearson's correlation analysis was performed for the correlation analysis. The total survival time was estimated using the Kaplan-Meier (K-M) survival curve, and was explored using the Log-ranch test.  $P < 0.05$  indicated significant differences.

## Results

*LINC00630 was highly expressed in colon carcinoma tissues and cells*

To verify the expression of LINC00630 in colon carcinoma, we pooled The Cancer Genome Atlas (TCGA) database [19] and found that the expression of LINC00630 was significantly elevated in cancer tissues. Then, we detected LINC00630 in tumor tissues and colon carcinoma cells using qRT-PCR and found that LINC00630 was significantly upregulated, suggesting that it may be involved in colon carcinoma. In addition, we divided the patients into high and low LINC00630 expression groups and analyzed their overall survival time. The survival time of patients with high LINC00630 was significantly shorter than those in low

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LINC00630 group, indicating that LINC00630 can be used as a potential prognostic indicator in colon carcinoma (**Figure 1**).

*Knocking down LINC00630 inhibited the proliferation and glycolysis of colon carcinoma cells and promoted apoptosis*

To determine the mechanism of LINC00630 in colon carcinoma cells, we first constructed three siRNA-LINC00630 plasmids and then transferred them into colon carcinoma cells, and si-LINC00630#1 exhibited the most significant inhibitory effect, which was used for the subsequent experiments (**Figure 2A, 2B**). CCK-8 and Flow cytometry experiments then revealed that the proliferation of cells transfected with si-LINC00630#1 was remarkably reduced, while the apoptosis was significantly increased (**Figure 2C, 2D**). In addition, we found that glucose consumption, lactic acid production, and PK activity of cells transfected with si-LINC00630#1 were decreased significantly (**Figure 2E**). These findings signify that LINC00630 knockdown can prevent the growth of colon carcinoma cells by inhibiting glycolysis.

*LINC00630 could be applied as a miR-409-3p sponge*

In earlier studies, it has been reported that lncRNA acts as a miR sponge. In this research, we found a targeted binding correlation between LINC00630 and miR-409-3p through starBase (**Figure 3A**) [20]. To test the correlation, we used qRT-PCR to detect miR-409-3p expression in tumors and revealed that the miR-409-3p expression was declined in tumors and negatively correlated with LINC00630 (**Figure 3B-D**). In addition, dual-luciferase report analysis revealed that the fluorescence activity of LINC00630-wt was noticeably inhibited by miR-409-3p-mimics (**Figure 3E**). The RIP pull-down test revealed that LINC00630 and miR-409-3p were precipitated via the Ago2 antibody (**Figure 3F**). Furthermore, qRT-PCR detection revealed that miR-409-3p was elevated in cells transfected with si-LINC00630#1 (**Figure 3G**). These results indicate that LINC00630 can act as a sponge of miR-409-3p.

*miR-409-3p targeted HK2*

It has been confirmed by many studies that miR regulates the downstream target genes involved in tumor glycolysis. HK2 was found to

be downstream gene of miR-409-3p (**Figure 4A**), and HK2 in colon carcinoma was shown to be elevated significantly in GEPIA (**Figure 4B**). In this study, qRT-PCR analysis revealed that HK2 was elevated in the tumor tissues of colon carcinoma (**Figure 4C**). Correlation analysis revealed that HK2 was positively correlated with LINC00630 but was negatively correlated with miR-409-3p (**Figure 4D**). Furthermore, dual-luciferase report experiments suggested that the fluorescence activity of HK2-WT was significantly inhibited by miR-409-3p-mimics transfection, and qRT-PCR and WB experiments revealed that mRNA and protein expressions of HK2 in colon carcinoma cells were significantly inhibited by transfection with miR-409-3p-mimics (**Figure 4E, 4F**). These experiments indicate that miR-409-3p targets HK2.

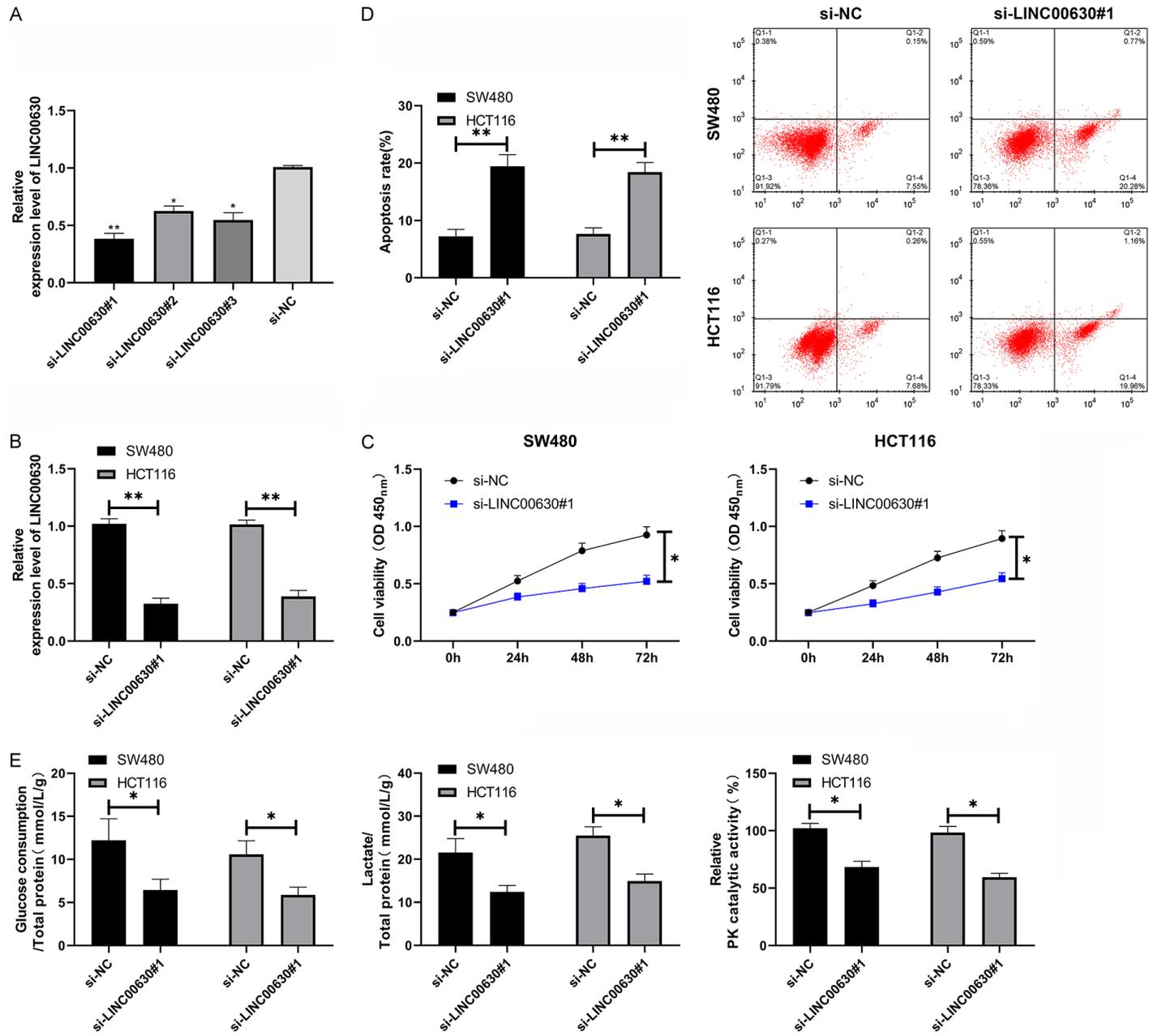
*Upregulating LINC00630 inhibited miR-409-3p on HK2 and promoted glycolysis*

To verify the regulatory role of LINC00630 in the miR-409-3p/HK2 axis, a rescue experiment was conducted to observe the growth and glycolysis of colon carcinoma. The results implied that co-transfection with miR-409-3p-mimics or si-HK2 significantly inhibited the proliferation or promoted apoptosis of cells transfected with pcDNA-LINC00630 (**Figure 5A, 5B**). In addition, we found that co-transfection inhibited glucose consumption, lactic acid production, and the PK activity of colon carcinoma cells, suggesting that LINC00630 can promote the occurrence of colon carcinoma by regulating miR-409-3p/HK2 axis (**Figure 5C**).

*LINC00630 inhibited the growth of colon carcinoma via the miR-409-3p/HK2 axis*

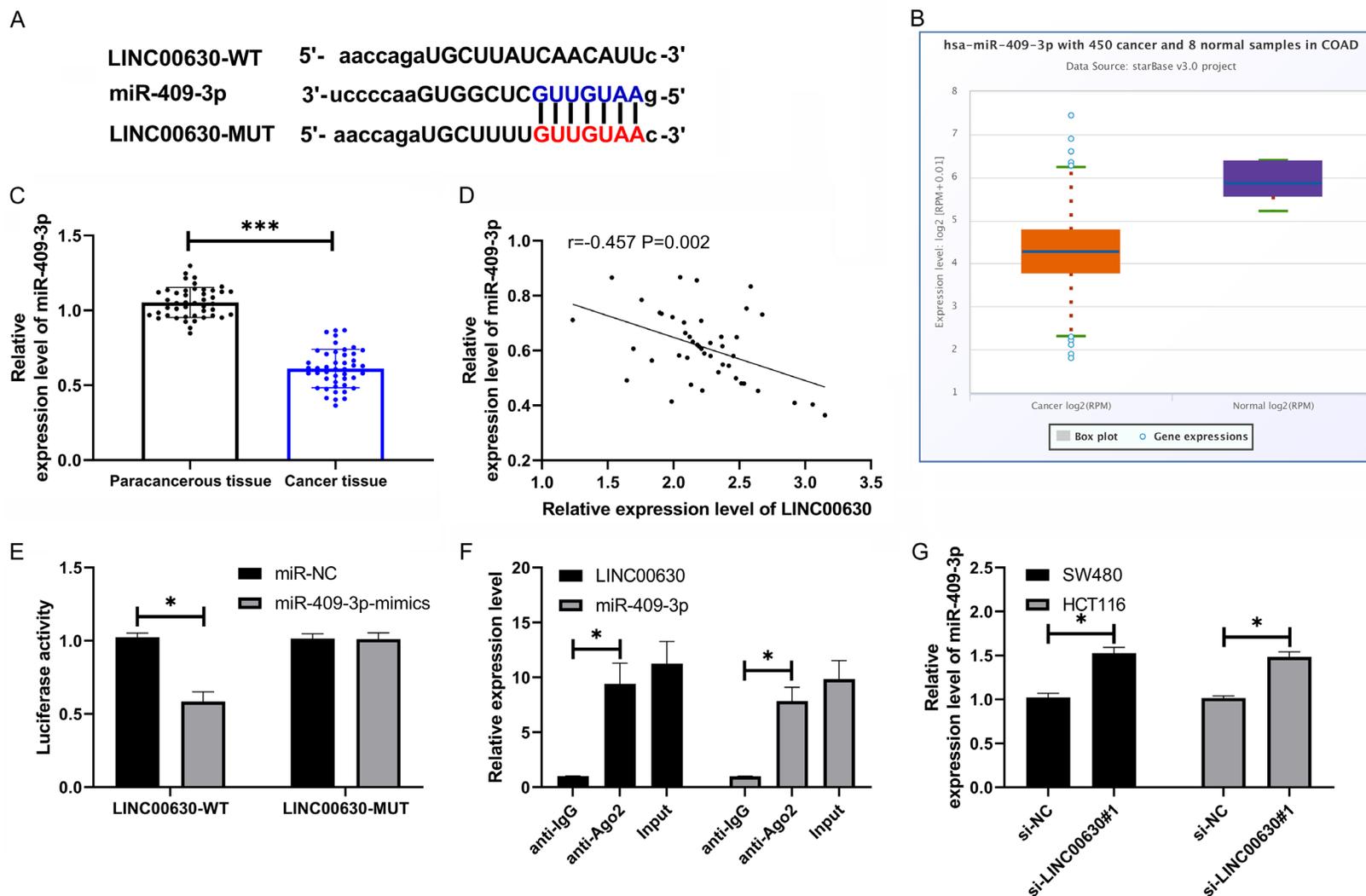
Finally, we established a tumor xenotransplantation model in nude mice. Observations revealed that the tumor volume and mass of nude mice were remarkably reduced after transfection of sh-LINC00630, indicating that knocking down LINC00630 could inhibit the growth of colon carcinoma (**Figure 6A, 6B**). In addition, tumor tissues were obtained for further analysis, and qRT-PCR showed that the expression of miR-409-3p was significantly elevated and the expression of HK2 was declined in nude mice infused with sh-LINC00630, establishing that LINC00630 knockdown can inhibit the growth of colon carcinoma via the miR-409-3p/HK2 axis (**Figure 6C**).

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## LINC00630 promotes apoptosis and glycolysis of colon carcinoma cells

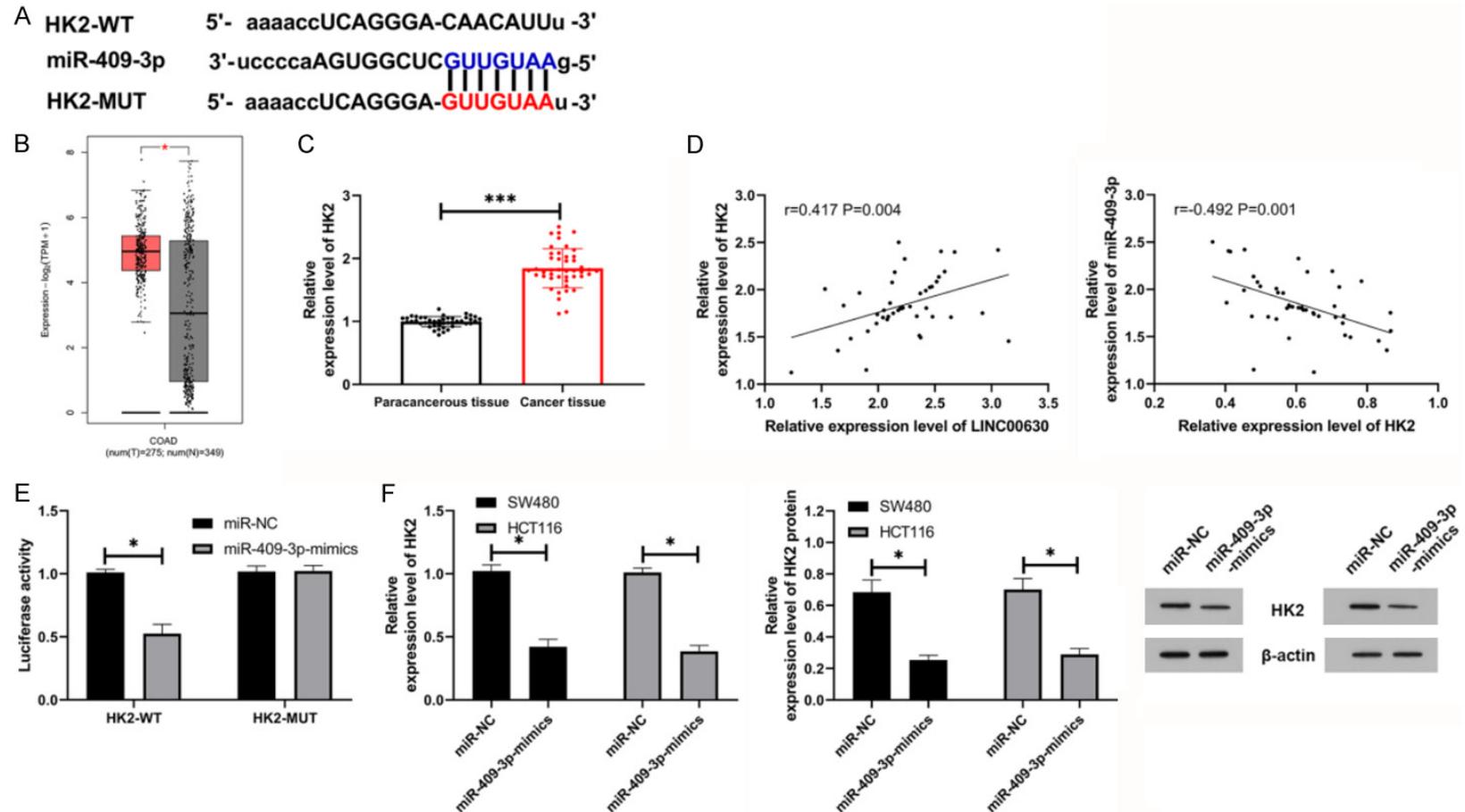
**Figure 2.** Effect of LINC00630 on the glycolysis of colon carcinoma. A. qRT-PCR was applied to test the LINC00630 plasmid after constructing si-LINC00630. B. qRT-PCR was applied to detect LINC00630 in colon carcinoma cell lines transfected with si-LINC00630#1. C. CCK-8 test was applied to detect changes in cell proliferation after transfection of si-LINC00630#1. D. Flow cytometry was applied to test the change in apoptosis after transfection of si-LINC00630#1. E. Changes in glucose consumption, lactic acid production, and PK activity in cells transfected with si-LINC00630#1. \*indicates  $P < 0.05$ ; \*\*indicates  $P < 0.01$ .



**Figure 3.** Verification of the targeting correlation of LINC00630 with miR-409-3p. A. starBase was applied to predict the target sites and mutation sites of LINC00630 and miR-409-3p. B. starBase was applied to test the online analysis of miR-409-3p in TCGA. C. qRT-PCR was applied to test miR-409-3p in the tumor tissues of

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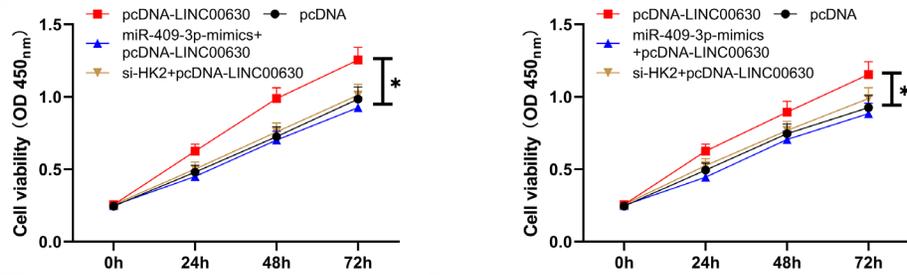
patients with colon carcinoma. D. Pearson's analysis was applied to test the correlation of LINC00630 with miR-409-3p in tumor tissues of patients with colon carcinoma. E. Dual-luciferase reporter was applied to test the targeted binding of LINC00630 with miR-409-3p. F. RIP experiment was applied to test the targeted binding of LINC00630 with miR-409-3p. G. qRT-PCR was applied to test miR-409-3p in colon carcinoma cells transfected with si-LINC00630#1. \*indicates  $P < 0.05$ ; \*\*\*indicates  $P < 0.001$ .



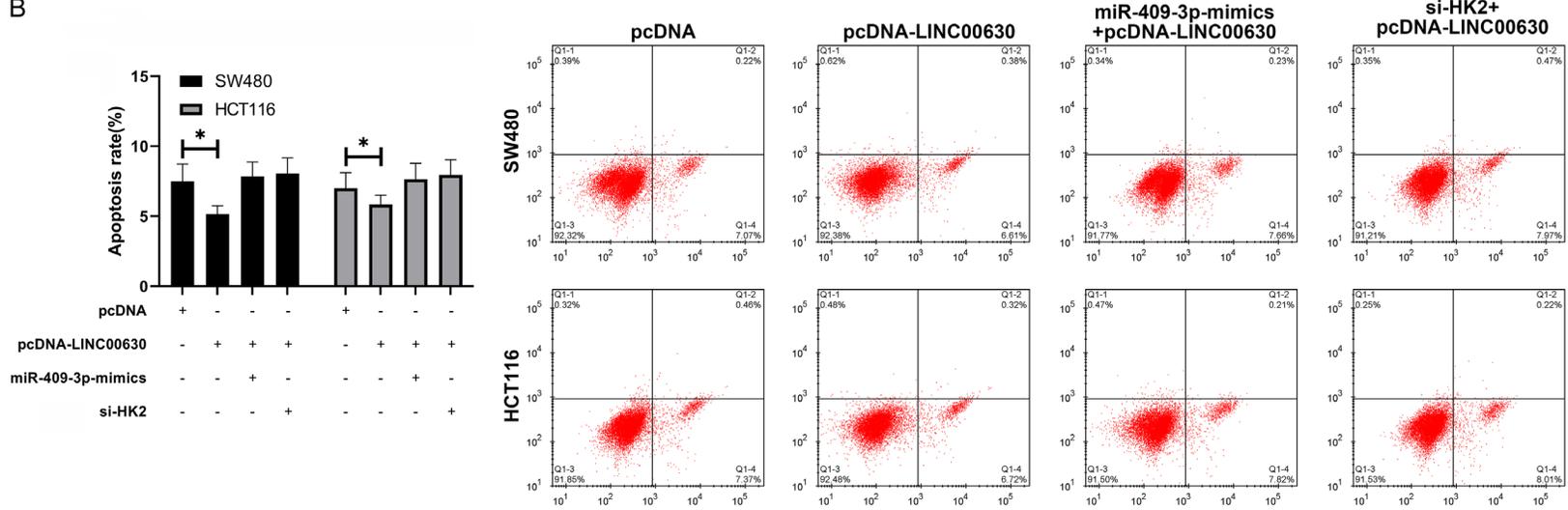
**Figure 4.** miR-409-3p could target HK2. A. starBase was applied to predict the target sites and mutation sites of miR-409-3p and HK2. B. GEPIA was applied to test HK2 of colon carcinoma in TCGA. C. qRT-PCR was applied to predict HK2 in tumor tissues of patients with colon carcinoma. D. Pearson's analysis was applied to predict the correlation of HK2 with LINC00630, and the miR-409-3p expression in tumor tissues of patients with colon carcinoma. E. Dual-luciferase reporter analysis of targeted binding between HK2 and miR-409-3p. F. qRT-PCR and WB were applied to test HK2 mRNA and protein in colon carcinoma cells transfected with miR-409-3p-mimics. \*indicates  $P < 0.05$ ; \*\*\*indicates  $P < 0.001$ .

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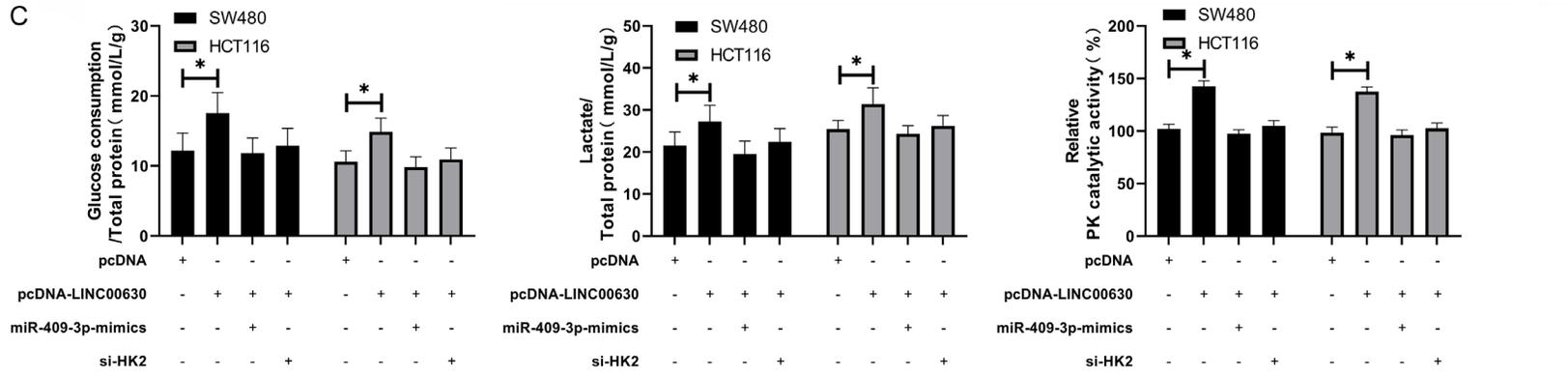
A



B

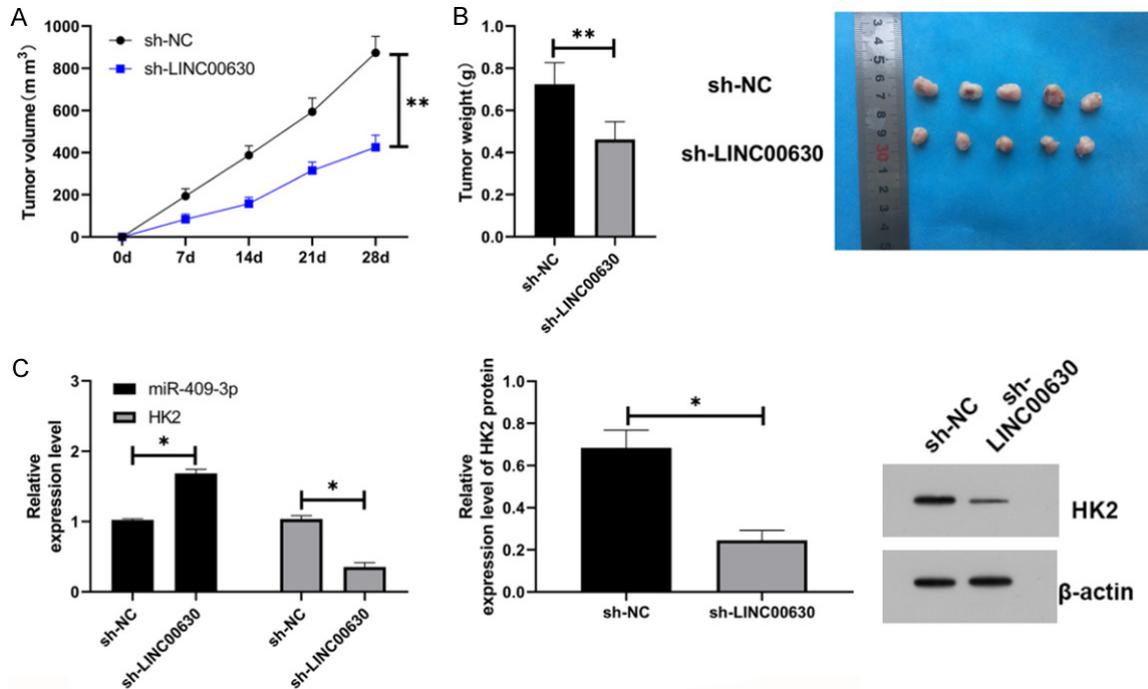


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## LINC00630 promotes apoptosis and glycolysis of colon carcinoma cells

**Figure 5.** LINC00630 mediated the regulation of the miR-409-3p/HK2 axis to promote glycolysis. A. CCK-8 experiment was applied to test the change in the cell proliferation ability after co-transfection. B. Flow cytometry showed the change in apoptosis after co-transfection. C. Changes in glucose consumption, lactic acid production, and PK activity in cells after co-transfection. \*indicates  $P < 0.05$ .



**Figure 6.** LINC00630 inhibited the growth of colon carcinoma via the miR-409-3p/HK2 axis. A. The change in tumor growth volume in nude mice within 28 days. B. After 28 days, the tumor tissue was collected and weighed. C. miR-409-3p, HK2 mRNA, and protein in tumor tissues were detected using qRT-PCR and WB. \*indicates  $P < 0.05$ ; \*\*indicates  $P < 0.01$ .

### Discussion

Colon carcinoma is a common malignancy characterized by distant metastasis and invasion and accounts for one-tenth of all tumor-related deaths [21]. LINC00630 was found to be elevated in colon carcinoma and could inhibit tumor growth by mediating the miR-409-3p/HK2 axis to regulate glycolysis, suggesting that LINC00630 may be a potential therapeutic target for colon carcinoma.

In recent years, more and more studies have revealed that carcinoma cells have a unique metabolic phenotype marked by increased glucose absorption and lactate release to support their malignant biological functions [22]. In addition, lncRNAs have a correlation with the Warburg effect [23, 24]. LINC00630 is a newly discovered lncRNA. At present, there are relatively few studies on the correlation of LINC00630 with colon carcinoma. TCGA data analy-

sis indicated that LINC00630 was elevated in colon carcinoma. It was verified that LINC00630 was elevated in tumor tissues and cell lines, and the 5-year survival rate was poor in patients with a high LINC00630 expression. This finding suggests that LINC00630 participates in the progression of colon carcinoma and may serve as a prognostic marker. Then, we knocked down LINC00630 in colon carcinoma cells. Observation hinted that the proliferation of colon carcinoma cells was noticeably inhibited, apoptosis was induced after transfection of si-LINC00630#1, and glucose consumption, lactic acid production, and the PK activity were declined significantly. These findings indicate that LINC00630 knockdown may prevent the growth of colon carcinoma cells by inhibiting glycolysis.

lncRNA, as a ceRNA, competitively binds to miRNA, thereby regulating the protein level of coding genes and the biological behavior of

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cells [25, 26]. For instance, Fan et al. [27] revealed that lncRNA CCAT1 was a competitive endogenous RNA in melanoma that was upregulated by ITGA9 through sponge of miR-296-3p. In this experiment, miR-409-3p was found to be a downstream gene of LINC00630. As an early-discovered miR, miR-409-3p was proved involving in the progression of colon carcinoma. Bai et al. [28] found that miR-409-3p partially inhibited the invasion and metastasis of colon carcinoma by targeting GAB1, while another study [29] revealed that miR-409-3p made colon carcinoma cells sensitive to oxaliplatin by inhibiting Beclin-1-mediated autophagy. Furthermore, we verified that the expression of miR-409-3p was decreased in the tumors of colon carcinoma patients, which is consistent with previous conclusions. Correlation analysis also revealed that miR-409-3p had a negative correlation with LINC00630. In addition, dual-luciferase reporter, RIP and the detection of transfected si-LINC00630#1 confirmed that LINC00630 could be used as a sponge for miR-409-3p. Moreover, HK2 was found to be downstream gene of miR-409-3p. As the first step in most glucose metabolic pathways, HK2 plays a role in catalyzing the phosphorylation of hexose, which is located on the outer membrane of mitochondria [30-32]. A previous study has shown that HK2 improves the glycolysis rate in rapidly growing carcinoma cells [33]. Our research showed that miR-409-3p could target HK2, suggesting that LINC00630 may regulate the glycolysis of colon carcinoma by mediating the miR-409-3p/HK2 axis, thereby regulating tumor growth.

To determine the correlation among LINC00630, miR-409-3p, and HK2, we conducted a rescue experiment and found that after transfection of pcDNA-LINC00630, the proliferation of cells was enhanced, and the apoptosis was inhibited, which were reversed by co-transfection of miR-409-3p-mimics or si-HK2. In addition, we also found that co-transfection inhibited glucose consumption, lactic acid production, and the PK activity of colon carcinoma cells, indicating that LINC00630 could promote the occurrence of colon carcinoma by regulating miR-409-3p/HK2 axis. In the final stage of this study, we established a nude mouse model and found that knockout of LINC00630 inhibited the growth of nude mice tumors by mediating the miR-409-3p/HK2 axis. These experiments revealed that LINC00630 was involved in the occurrence of colon carcinoma.

This study confirmed the role of LINC00630 in colon carcinoma, but some limitations do exist. First, whether LINC00630 can be used as a prognostic indicator of colon carcinoma is yet to be verified using a large sample of clinical data. Second, early studies have found that glycolysis is closely related to the drug resistance of tumor cells. We did not explore the role of LINC00630 in colon carcinoma drug resistance. Therefore, we hope to perform more experiments in the future and validate our research findings.

In conclusion, LINC00630 is elevated in colon carcinoma and its downregulation inhibits the growth of colon carcinoma via the miR-409-3p/HK2 axis, which may be a potential target for colon carcinoma treatment.

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### Disclosure of conflict of interest

None.

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