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OCT1 regulates the migration of colorectal cancer cells by acting on LDHA

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Summary. Colorectal cancer is one of the most common cancers with high morbidity and mortality. Effective treatments to improve the prognosis are still lacking. The results of online analysis tools showed that OCT1 and LDHA were highly expressed in colorectal cancer, and the high expression of OCT1 was associated with poor prognosis. Immunofluorescence demonstrated that OCT1 and LDHA co-localized in colorectal cancer cells. In colorectal cancer cells, OCT1 and LDHA were upregulated by OCT1 overexpression, but downregulated by OCT1 knockdown. OCT1 overexpression promoted cell migration. OCT1 or LDHA knockdown inhibited the migration, and the downregulation of LDHA restored the promoting effect of OCT1 overexpression. OCT1 upregulation increased the levels of HK2, GLUT1 and LDHA proteins in colorectal cancer cells. Consequently, OCT1 promoted the migration of colorectal cancer cells by upregulating LDHA.

Key words: Colorectal cancer, OCT1, LDHA, Migration

Introduction

Colorectal cancer is one of the most common cancers, with an incidence rate of third in the world and the second in mortality rate, accounting for about 10% of global cancer cases and cancer-related deaths (Sung et al., 2021). The distribution of colorectal cancer is different among women and men, with the incidence rate and mortality rate of women being about 25% lower than that of men. The incidence rate is also different in geography, and the incidence rate in developed countries is higher (Arnold et al., 2017; Bray et al., 2018). In addition to the aging population and the eating habits of high-income countries, unfavorable risk factors that increase the risk of colorectal cancer include obesity, lack of physical exercise and smoking (Dekker et al., 2019). So far, the treatment methods of colorectal cancer include surgical resection, radiotherapy, chemotherapy, targeted therapy and immunotherapy (Punt et al., 2017). Effective treatments such as early diagnosis and endoscopic resection have improved the survival rate of patients (Liu et al., 2021). However, most patients are already in the advanced stage of colorectal cancer at the time of diagnosis. At this time, the patients are resistant to most forms of combination therapy. Despite radical resection, the prognosis is still very poor, and recurrence occurs during treatment (La Vecchia and Sebastian, 2020). These adverse treatment results indicate the need to better understand the molecular mechanism of colorectal cancer progression.

Octamer transcription factor 1 (OCT1; Gene symbol POU2F1) is one of the earliest described mammalian transcription factors and a widely expressed POU domain transcription factor, which is related to OCT4, the master transcription factor of embryonic stem cells (Herr et al., 1988). Takuya Ogura et al. proposed that OCT1 was highly expressed in estrogen receptor (ER)-positive breast cancer tissues and directly combined with NCAPH promoter to stimulate the transcription of NCAPH (Ogura et al., 2021). OCT1 not only plays a carcinogenic role in gastric cancer and precancerous lesions, but also promotes the proliferation and migration of gastric cancer and epithelial-mesenchymal transition (EMT) (Qian et al., 2015; Liang et al., 2020). In addition, the high expression of OCT1 in prostate cancer tissue is associated with an adverse prognosis (Obinata et al., 2012). However, understanding of the role of OCT1 in colorectal cancer and regulation

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mechanisms are not clear enough.

According to the relevant data analysis in the public database, this study found that the expression of OCT1 was upregulated in colorectal cancer, and was associated with a poor prognosis. We further determined the effect of OCT1 overexpression or knockdown on the migration of colorectal cancer cells, and initially explored the molecular regulatory mechanism of OCT1 in colorectal cancer.

Materials and methods

Cell culture

Human colorectal cancer cell lines (Caco-2, SW480 and HCT 116) and normal colorectal mucosal cells (FHC cells) were purchased from BeNa Biotech (Beijing, China), and cultured in DEMD high glucose medium (Hyclone) supplemented with 10% fetal bovine serum (FBS) (GIBCO). All cells were cultured in a 37°C incubator with 5% CO_2.

Public Database

UALCAN (http://ualcan.path.uab.edu) and ENCORI (http://starbase.sysu.edu.cn/index.php) databases were used to analyze the mRNA levels of OCT1 and LDHA in colorectal cancer tissues and normal tissues (Yang et al., 2011; Li et al., 2014; Chandrashekar et al., 2017, 2022). UALCAN database was also applied to evaluate the relationship between OCT1 and the survival of colorectal cancer patients. Using the UALCAN web-portal, we analyzed the mRNA levels of OCT1 and LDHA in 286 colorectal cancer and 41 normal tissue samples from TCGA database. There were 471 colorectal cancer samples and 41 normal samples in ENCORI database, which were used to analyze the expression of OCT1 and LDHA. Human Protein Atlas (https://www.proteinatlas.org) was employed to assess the protein expression levels of OCT1 and LDHA in colorectal cancer tissues and normal colon tissues (Uhlen et al., 2005, 2015; Ponten et al., 2008). In Human Protein Atlas, 6 colon tissues and 22 colorectal cancer tissues were used to assess OCT1 protein levels, and 5 colon tissues and 20 colorectal cancer tissues were used to detect LDHA protein levels.

Colorectal cancer cell models with gene overexpression or knockdown

Primer amplification sequences and RNA interference target gene sequences were designed using OCT1 gene as template. Primer amplification sequences were amplified by PCR to prepare the target gene fragment. RNAi target sequences were synthesized into single-stranded DNA oligo, which was paired to produce double-stranded DNA after annealing. Then the amplified target gene fragment or double-stranded DNA containing interference sequence was inserted into a lentiviral vector. Caco-2 and SW480 cells were infected with OCT1 overexpression lentiviral vector to construct OCT1 overexpression colorectal cancer cell models. HCT 116 cells were infected with lentiviral vector containing OCT1 interference sequence to construct OCT1 knockdown colorectal cancer cell model. The target sequence of OCT1 gene interference was as follows: ATGGAAATGACTTCAGCCAAA.

RT-qPCR

Real time quantitative PCR detection system (RT-qPCR) was performed to detect the expression of OCT1 and LDHA mRNA in colorectal cancer cells. Colorectal cancer cells infected with different lentiviruses were collected and centrifuged to obtain the cell pellets. Total RNA was extracted from colorectal cancer cells by Trizol kit (T9424-100m, Sigma). According to the manufacturer's instructions, RNA was reverse transcribed to obtain cDNA by using Hiscript QRT supermax for qPCR (+ gDNA WIPER) kit (R123-01, Vazyme). Subsequently, SYBR Green master mix (Q111-02, Vazyme), forward and reverse primers, cDNA and other reagents were configured in proportion to the reaction system, and the Real time PCR instrument (VII7, ABI) was used for detection in a two-step method. Finally, $2^{-\Delta\Delta Ct}$ was used to calculate the relative expression of gene mRNA. GAPDH was used as an internal reference.

Forward primer of OCT1: 5' ACTTCCACAGA GCCAGTCAACA 3', reverse primer of OCT1: 5' ATAGCGAGCCCAACATCACC 3'; Forward primer of LDHA: 5' CAGCCTTTTCCTTAGAACACCA 3', reverse primer of LDHA: 5' TGTTCACGTTACG CTGGACC 3'; Forward primer of GAPDH: 5' TGACTTCAACAGCGACACCCA 3', reverse primer of GAPDH: 5' CACCCTGTTGCTGTAGCCAAA 3'.

Transwell assay

100 μl serum-free medium was added to the upper Transwell chamber (3422, Corning) and the medium was removed after being placed in the 37°C incubator for 2h. 100 μl of colorectal cancer cell suspension (containing 2.5×10^4 Caco-2 cells or 8×10^4 SW480 cells or 8×10^4 HCT 116 cells) was added to the upper chamber, and then the upper chamber was transferred to the lower chamber supplemented with 600 μl medium containing 30% FBS. After 48h, the upper chamber was taken out and non-migration cells were gently removed with a cotton swab. The upper chamber was placed in the lower chamber with 400 μl Giemsa for 5 min to stain the transferred cells. Finally, the upper chamber was rinsed with water and dried. The pictures were taken with a microscope (IX 73, Olympus), and the metastatic colorectal cancer cells were counted.

Immunofluorescence staining assay

The prepared cell glass slides were fixed with 4%

paraformaldehyde for 15 min. The glass slides were washed with PBS 3 times for 3 min each time. Then 0.5% Triton X-100 (Sigma) was used to permeate at room temperature for 20 min. The glass slides were washed with PBS 3 times for 3 min each time. After blotting the PBS on the slides with absorbent paper, the cells were blocked with goat serum at room temperature for 30 min. After absorbing the serum with absorbent paper, the cells were incubated with primary antibody at 4°C overnight. 1×PBST was used to clean the glass slides 3 times for 5 min each time. The cells were incubated with fluorescent secondary antibody at 37°C for 30 min. 1×PBST was used to clean the glass slides 3 times for 5 min each time, and the PBST was removed with absorbent paper. DAPI was added to stain the nucleus for 5 min in the dark. The glass slides were sealed with aqueous mounting medium, and then the edges of the glass slides were sealed with neutral gum. The glass slides were photographed with different wavelengths of light by using a fluorescence microscope (IX 73, Olympus) to analyze the expression of antibodies in cells.

The relevant antibody information was as follows: OCT1 (1:200), ab51363, adcam; Alexa Fluor® 488 labeled Goat anti-mouse IgG (H+L) (1:200), ab150113, abcam; LDHA (1:100), 3582T, CST; Alexa Fluor® 594 labeled Goat anti-rabbit IgG (H+L) (1:200), ab150080, abcam; mounting medium with DAPI-Aqueous, Fluoroshield, ab104139, abcam.

Western blot

Total protein was extracted from colorectal cancer cells infection with lentivirus. BCA Protein Assay Kit (23225, HyClone-Pierce) was used to detect protein concentration. 20 μg protein was subjected to SDS-PAGE by using SDS-Acryl/Bis protein electrophoresis instrument (VE-180, Shanghai Tianneng), and the proteins were transferred to PVDF membrane. 1×TBST solution containing 5% skimmed milk was used to block the PVDF membrane at room temperature for 1h. The diluted primary antibodies were incubated with PVDF membrane at room temperature for 2h. The PVDF membrane was cleaned 3 times with 1×TBST solution, 10 min each time. Then PVDF membrane was incubated in the secondary antibodies at room temperature for 1h. After cleaning PVDF membrane with 1×TBST solution 3 times, the proteins on the PVDF membrane were developed color with immobilon Western chemi-lumenescent HRP Substrato Kit (RPN2232, Millipore). Chemiluminescence was performed with a Chemi-luminescence Imager (AI600, GE).

The information of the relevant primary and secondary antibodies was as follows: OCT1 (1:1000), rabbit, bs-1075R, Bioss; HK2 (1:2000), rabbit, 22029-1AP, Proteintech; GLUT1 (1:1000), rabbit, 21829-1-AP, Proteintech; LDHA (1:1000), rabbit, 66287-1-lg, Proteintech; GAPDH (1:3000), rabbit, AP0063, Bioworld; HRP goat anti-rabbit IgG antibody (1:3000),

A0208, Beyotime.

Statistical analysis

The relevant cell experiments in this study were repeated three times. All data were expressed as average ± Standard deviation (SD). SPSS software was used for statistical analysis of data results, and GraphPad Prism was used to draw statistical graphs. Student t-test was used for statistical analysis between the two groups. When P value was less than 0.05, the difference was statistically significant.

Results

OCT1 promoted the migration of colorectal cancer cells

Up to now, it had been reported that the expression of OCT1 was increased in colorectal cancer, and the increased expression of OCT1 was closely related to the low survival rate of colorectal cancer patients. It was worth noting that the down-regulation of OCT1 expression inhibited the proliferation of colorectal cancer cells (Wang et al., 2016). In this study, we found that mRNA levels of OCT1 in colorectal cancer were markedly higher than that in normal tissues (Fig. 1A,B). According to the Human Protein Atlas, OCT1 was lowly expressed in 6 colon tissues, while 19 out of 22 colorectal cancer tissues showed medium expression of OCT1 and one cancer tissue showed high expression (Fig. 1C). Besides, the higher the expression of OCT1 in colorectal cancer, the lower the survival probability of patients (Fig. 1D). Compared with normal colorectal mucosal cells (FHC cells), OCT1 was significantly upregulated in colorectal cancer cell lines (Caco-2, SW480 and HCT 116 cells), and the expression level of OCT1 was highest in HCT 116 cells (Fig. 1E). In order to further explore the role of OCT1 in colorectal cancer, lentivirus infection technology was applied to construct colorectal cancer cells with OCT1 overexpression or knockdown. RT-qPCR results showed that the levels of OCT1 mRNA in Caco-2 and SW480 cells infected with OCT1 lentivirus were obviously upregulated (Fig. 2A,B), but downregulated in HCT 116 cells infected with shOCT1 lentivirus (Fig. 2C). Further Transwell assay indicated that overexpression of OCT1 promoted the migration of colorectal cancer cells (Caco-2 and SW480 cells) (Fig. 2D,E), while knockdown of OCT1 significantly restricted the migration of colorectal cancer cells (HCT 116 cells) (Fig. 2F).

OCT1 promoted colorectal cancer cell migration by upregulating LDHA

The overexpression of OCT1 increased LDHA mRNA levels in colorectal cancer cells (Caco-2 and SW480 cells) (Fig. 3A). Accordingly, LDHA mRNA level was significantly down regulated by shOCT1 (Fig. 3A). Moreover, the results of immunofluorescence

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experiment revealed that OCT1 and LDHA proteins were co-localized in the cytoplasm of colorectal cancer cells (Caco-2, SW480 and HCT 116 cells) (Fig. 3B). These results suggested that OCT1 may play a role in colorectal cancer by acting on the expression of LDHA. We also found that LDHA mRNA had a higher expressed level in colorectal cancer (Fig. 4A,B). Human Protein Atlas data showed that LDHA was downregulated in 2 out of 5 colon tissues. Among 21 colorectal cancer tissues, LDHA was moderately expressed in 12 cancer tissues and highly expressed in 8 cancer tissues (Fig. 4C).

Besides, the expression of LDHA in SW480 cells was markedly decreased by shLDHA (Fig. 5A).
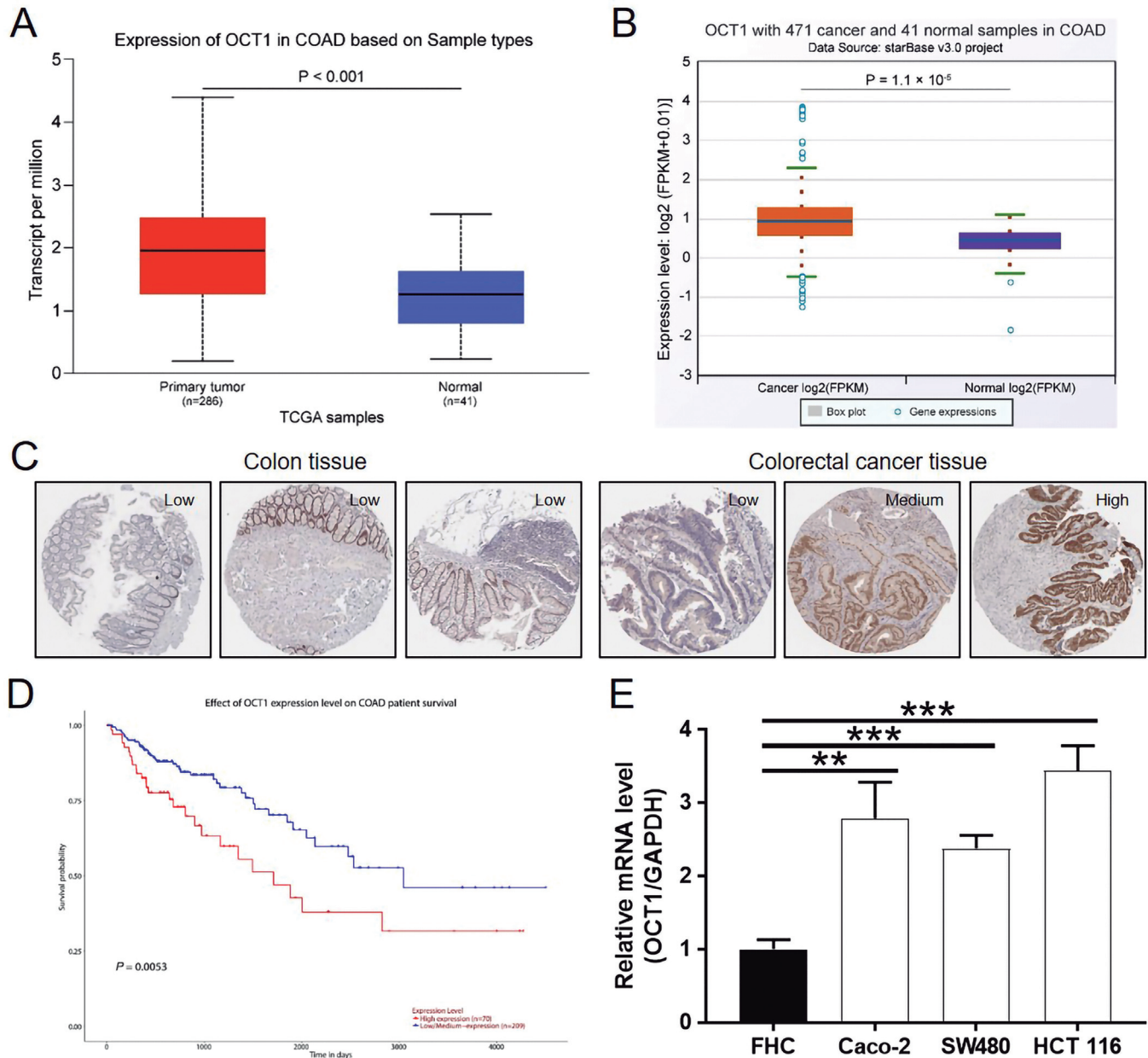
Fig. 1. OCT1 was highly expressed in colorectal cancer tissues. **A.** The expression levels of OCT1 mRNA in colon adenocarcinoma (CODA) and normal tissues were analyzed by TCGA data from UALCAN database. **B.** The expression of OCT1 mRNA in CODA and normal tissues was determined by TCGA data from ENCORI database. **C.** Human Protein Atlas was used to demonstrate the protein expression of OCT1 in colorectal cancer and normal colon tissues. **D.** TCGA data from UALCAN database were applied to evaluate the correlation between OCT1 expression and patient survival. **E.** The mRNA levels of OCT1 were detected by RT-qPCR and the expression of OCT1 was higher in colorectal cancer cell lines (Caco-2, SW480 and HCT 116 cells) than that in normal human colorectal mucosal cells (FHC cells). **P<0.01, ***P<0.001
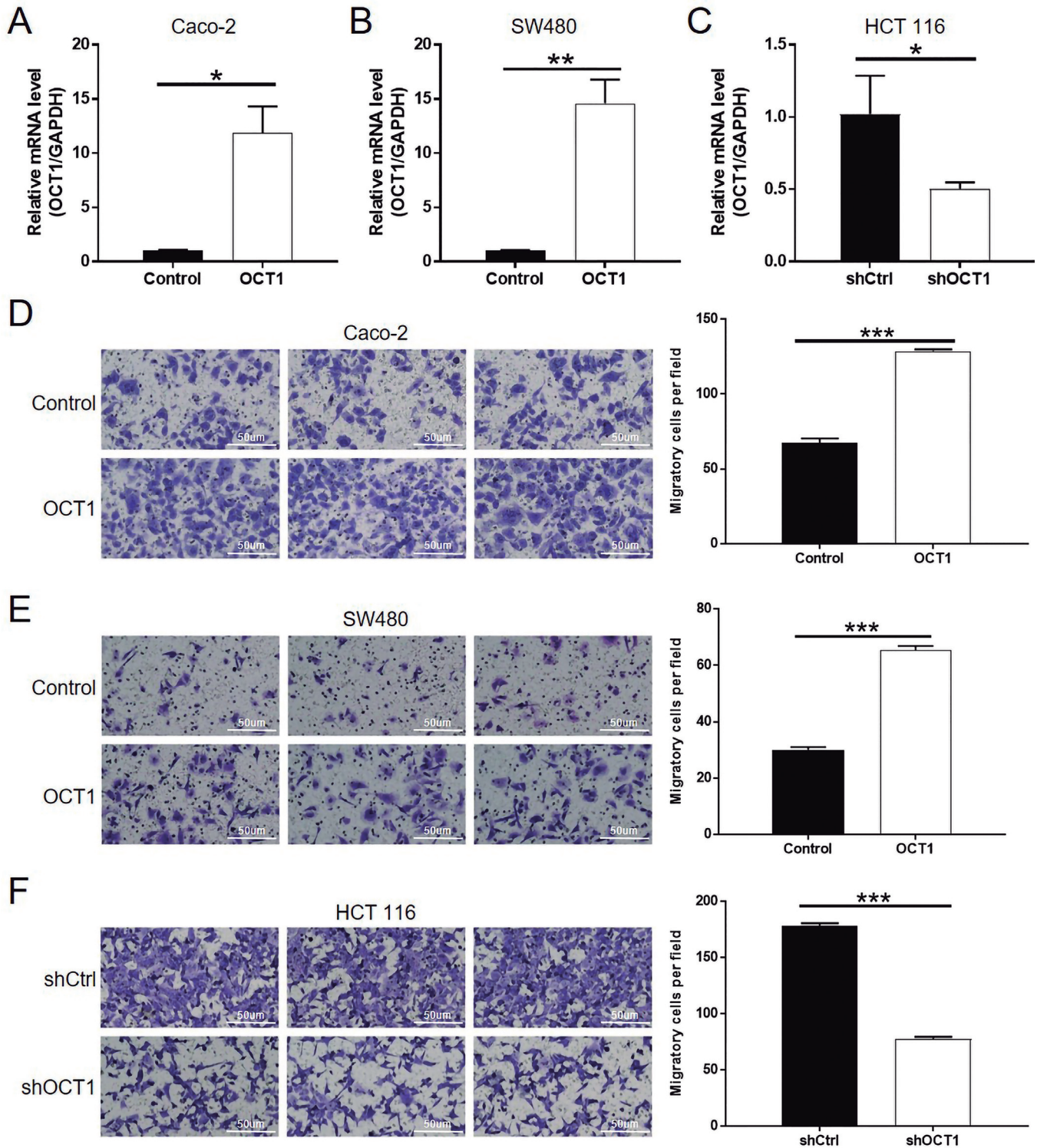
Fig. 2. OCT1 overexpression or knockdown colorectal cancer cell models were constructed and the migration was assessed. **A-C.** Colorectal cancer cell models with overexpression or knockdown of OCT1 were established by lentivirus infection technique. The expression levels of OCT1 mRNA in colorectal cancer after overexpression or knockdown of OCT1 were detected by RT-qPCR assay. **D-F.** Transwell assay was performed to determine the migration of colorectal cancer cells (Caco-2, SW480 and HCT116). Control: Colorectal cancer cells infected with empty vector, as negative control; OCT1: colorectal cancer cells infected with OCT1 lentivirus for overexpressing OCT1; shCtrl: colorectal cancer cells infected with empty vector, as negative control; shOCT1: colorectal cancer cells infected with shOCT1 lentivirus for downregulating OCT1. *$P<0.05$; **$P<0.01$. ***$P<0.001$. Scale bars: 50 µm.
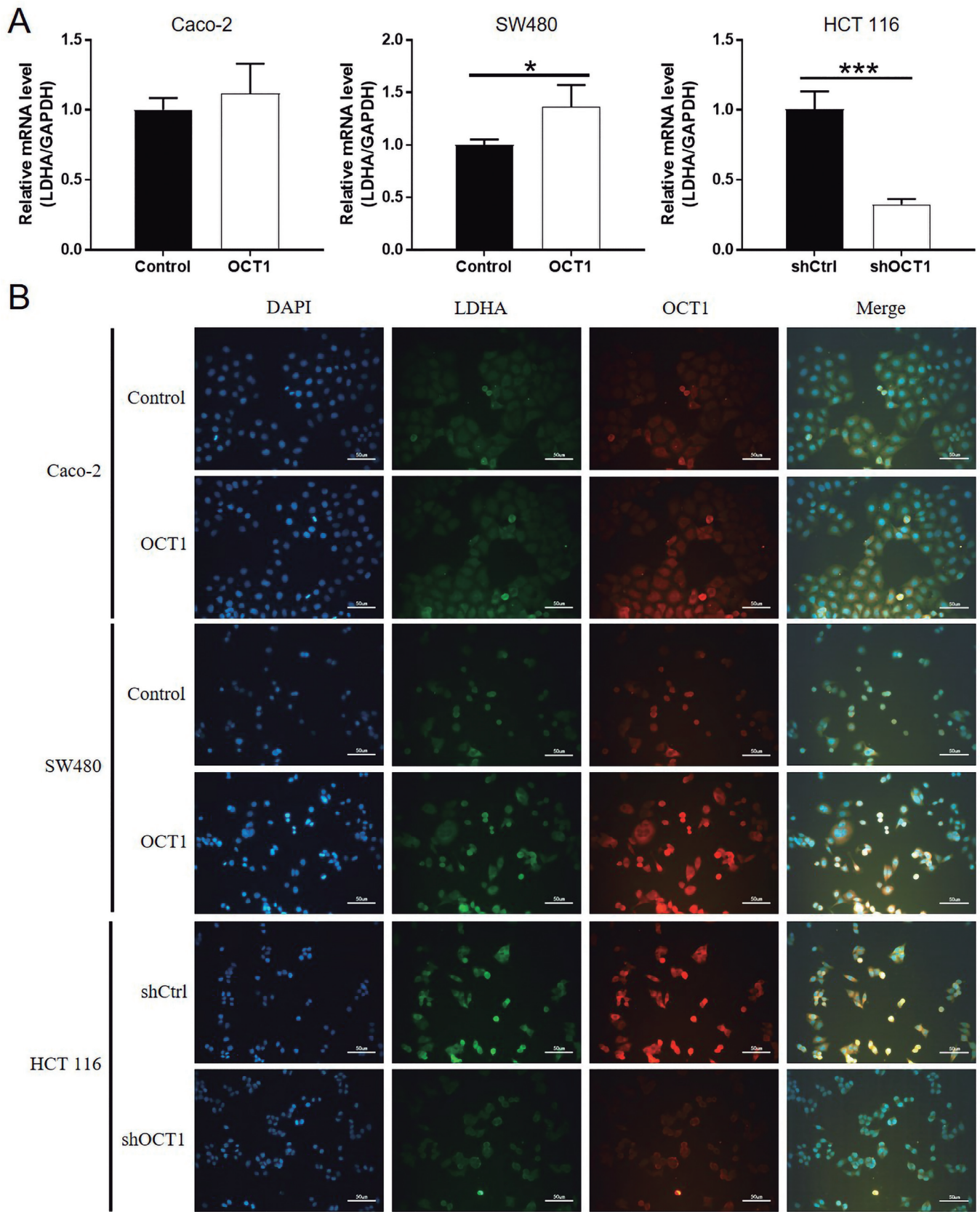
Fig. 3. OCT1 upregulated the expression of LDHA and co-localized with LDHA in the cytoplasm of colorectal cancer cells. **A.** The expression levels of LDHA mRNA in colorectal cancer after overexpression or knockdown of OCT1 were detected by RT-qPCR assay. **B.** The co-localization of OCT1 and LDHA in colorectal cancer cell lines was analyzed by immunofluorescence assay. Control: Colorectal cancer cells infected with empty vector, as negative control; OCT1: colorectal cancer cells infected with OCT1 lentivirus for overexpressing OCT1; shCtrl: colorectal cancer cells infected with empty vector, as negative control; shOCT1: colorectal cancer cells infected with shOCT1 lentivirus for downregulating OCT1. $*P<0.05$; $***P<0.001$. Scale bars: 50 μm.

Upregulation of OCT1 also enhanced the expression of LDHA, and the level of LDHA in colorectal descended after infection with shLDHA lentivirus (Fig. 5B). OCT1 overexpression promoted the migration of SW480, while LDHA under-expression restrained the migration and partially restored the promoting migration caused by OCT1 overexpression (Fig. 5C). These results revealed that OCT1 promoted the migration of colorectal cancer cells by upregulating LDHA expression.

OCT1 might affect the glycolytic progress in colorectal cancer cells

As a glycolytic enzyme, LDHA was involved in glycolysis and gluconeogenesis. OCT1 regulated the expression of LDHA, therefore, we speculated that OCT1 might be involved in the regulation of colorectal cancer cell glycolysis. Western blot was performed to detect the expression of several glycolysis-related proteins. The results showed that OCT1 overexpression improved the levels of HK2, GLUT1 and LDHA proteins, and the levels of HK2 protein were decreased by OCT1 silence (Fig. 6A-C). Gray analysis of western blot results also demonstrated that OCT1 overexpression significantly upregulated HK2, GLUT1 and LDHA levels, and conversely, OCT1 knockdown significantly inhibited the expression of these glycolytic related proteins (Fig. 6A-C).

Discussion

Colorectal cancer, one of the most common cancers, is the second most common cause of cancer-related death around the world. However, the mechanisms leading to the occurrence and development of colorectal cancer are still unclear (Wang et al., 2020b). This study analyzed the expression levels of OCT1 in colorectal cancer, and found that OCT1 overexpression promoted the migration of colorectal cancer cells. Furthermore, OCT1 also affected the expression of LDHA and regulated the expression of glycolysis-related proteins, suggesting that OCT1 played a crucial role in colorectal cancer.

OCT1 had a role in promoting tumor progression in a variety of tumors, and also had potential prognostic and therapeutic significance for multiple types cancer, especially gastrointestinal tract, lung and breast cancer (Vazquez-Arreguin and Tantin, 2016). Shinichiro
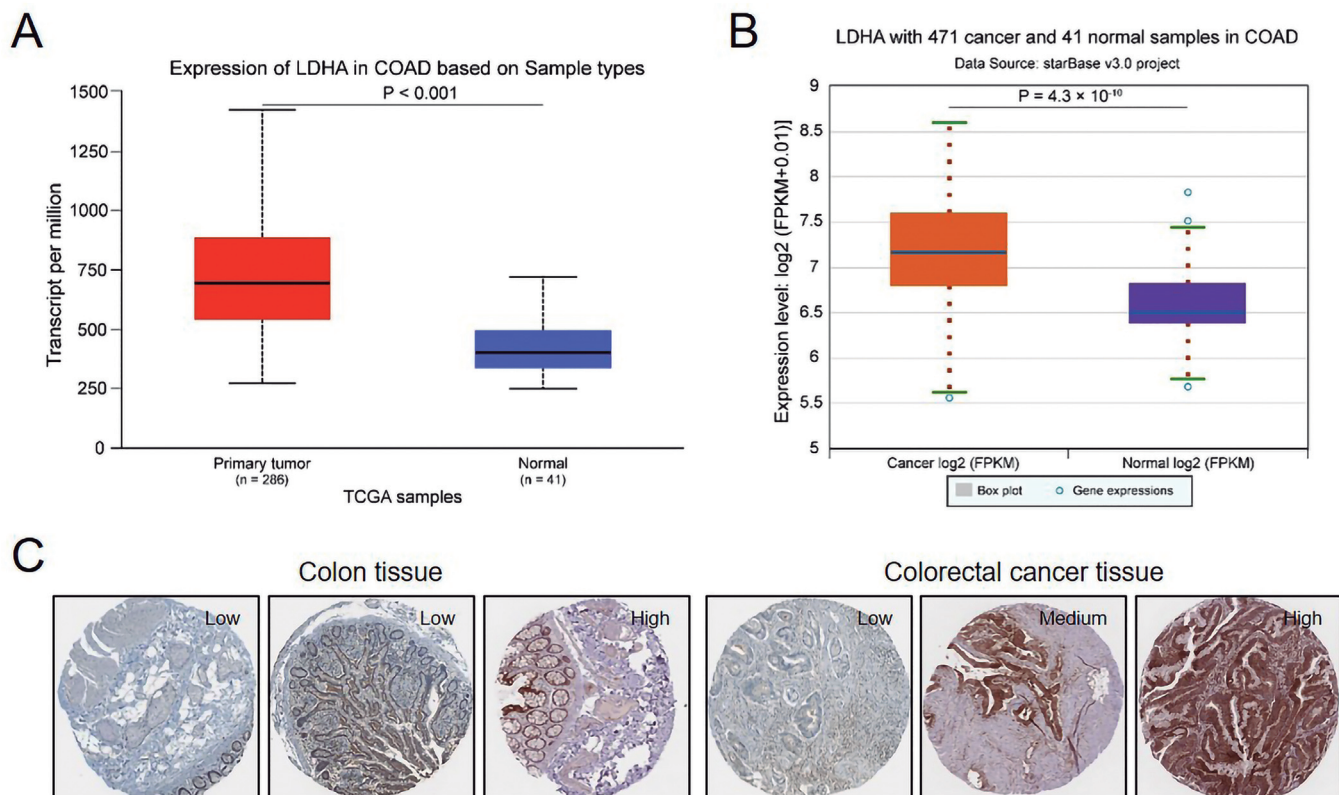

Fig. 4. LDHA was highly expressed in colorectal cancer tissues. **A.** The expression levels of LDHA mRNA in colon adenocarcinoma (CODA) and normal tissues were obtained from TCGA data in UALCAN. **B.** The expression of LDHA mRNA in CODA and normal tissues was demonstrated by TCGA data from ENCORI database. **C.** Human Protein Atlas website was used to determine the protein expression of LDHA in colorectal cancer and normal colon tissues.

Yamamoto et al. proposed that OCT1 was upregulated in castration-resistant prostate cancer, and knocking out OCT1 gene inhibited the proliferation and metastasis of castration-resistant prostate cancer cells (Yamamoto et al., 2019). In this study, according to the data analysis in UALCAN, ENCORI and Human Protein Atlas, the mRNA and protein levels of OCT1 were highly expressed in colorectal cancer tissues, and patients with high expression of OCT1 had a shorter survival time, which was consistent with the study of Yupeng Wang et al. that is, OCT1 was indeed highly expressed in colorectal cancer, and was correlated with overall survival (Wang et al., 2016). Besides, compared with FHC cells, OCT1 was overexpressed in Caco-2, SW480 and HCT 116 cells. In the present study, we not only constructed OCT1 overexpressing colorectal cancer cell (Caco-2 and SW480) models *in vitro*, but also established an OCT1 knockdown colorectal cancer cell (HCT 116) model. The expression of OCT1 mRNA in colorectal cancer cells was upregulated by OCT1 overexpression lentivirus, but downregulated by shOCT1 lentivirus. Moreover, forced overexpression of OCT1 promoted the migration of Caco-2 and SW480 cells, while knockdown of OCT1 restricted the migration of HCT 116 cells. These results indicated that OCT1 had a cancer-promoting effect in colorectal cancer.

LDHA (lactate dehydrogenase A) was an enzyme that catalyzed the conversion of pyruvate and NADH into lactic acid and NAD+, and played pivotal role in regulating glycolysis. LDHA was usually upregulated in cancer cells, promoting metabolism conversion to aerobic glycolysis, as well as cancer cell invasion and tumor metastasis (Jin et al., 2017). LDHA had a high expression in oral squamous cell carcinoma (OSCC), and as an oncogene, it promoted the malignant progression of OSCC by promoting glycolysis and EMT (Cai et al., 2019). Similarly, we found that LDHA mRNA and protein had higher expression levels in colorectal cancer. OCT1 overexpression upregulated the expression of LDHA mRNA in SW480 cells, and OCT1 silencing limited the expression of LDHA mRNA in HCT 116 cells. Furthermore, immunofluorescence assay
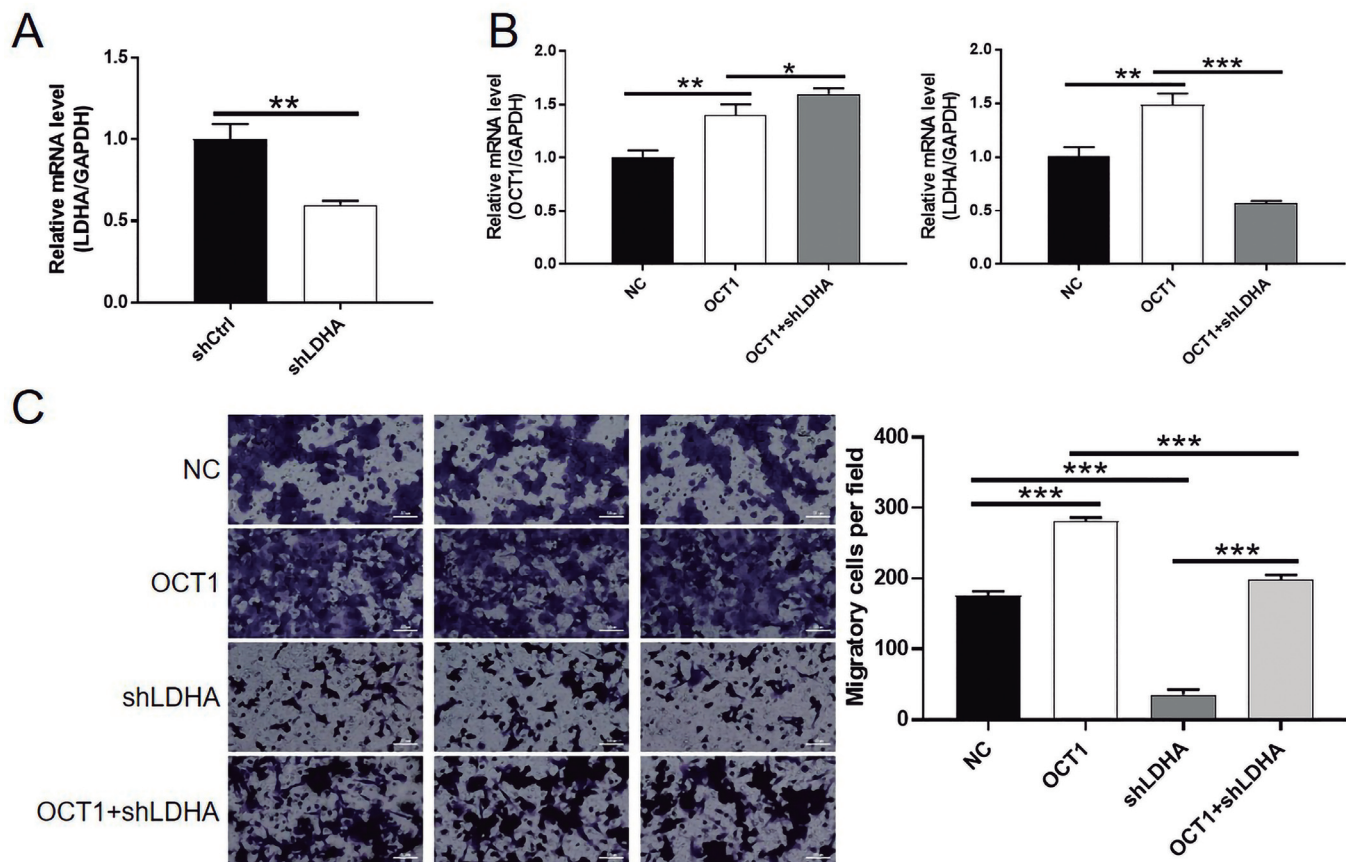

Fig. 5. OCT1 promoted the migration of colorectal cancer cells by upregulating LDHA. **A.** After SW480 cells infection with shLDHA lentivirus, the mRNA levels of LDHA were decreased. **B.** The expression of OCT1 and LDHA in SW480 cells were determined by RT-qPCR. **C.** Transwell assay was performed to determine the migration of SW480 cells with OCT1 overexpression or/and LDHA knockdown. NC: SW480 cells infected with empty vector, as negative control; OCT1: SW480 cells infected with OCT1 lentivirus for overexpressing OCT1; shCtrl: SW480 cells infected with empty vector, as negative control; shLDHA: SW480 cells infected with shLDHA lentivirus for downregulating OCT1; OCT1+shLDHA: SW480 cells infected with OCT1 and shLDHA lentiviruses. *$P<0.05$; **$P<0.01$. ***$P<0.001$. Scale bars: 50 μm.

showed that LDHA and OCT1 were co-localized in the cytoplasm of colorectal cancer cells. Therefore, we proposed that OCT1 might promote the migration of colorectal cancer cells by regulating the expression of LDHA. In SW480 cells with LDHA knockdown, the expression of LDHA was diminished and the cell migration ability was attenuated. OCT1 overexpression facilitated the expression and LDHA and cell migration, which was restricted by LDHA knockdown. Besides, under the regulation of hCINAP, LDHA promoted aerobic glycolysis and colorectal cancer progression (Ji et al., 2017).

Cell metabolism provided energy for cancer cells and was closely related to the fate and phenotype of cancer cells. Cell metabolism also controlled the epigenetic status of tumor cells and was the key to regulating tumor progression (Vander Heiden and DeBerardinis, 2017; Rinaldi et al., 2018). As an effective regulator of stress response, metabolism and tumorigenicity, the loss of OCT1 was related to increased oxidative metabolism, increased reactive oxygen species, hypersensitivity to oxidative and genotoxic stress, and a moderate increase in abnormal

mitosis, which can promote glycolytic metabolism and mitotic stability (Ng et al., 2010; Vazquez-Arreguin et al., 2019). Aerobic glycolysis was the main pathway of energy metabolism in cancer cells. In aerobic glycolysis, tumor cells absorbed and metabolized more glucose than normal tissues, and even in aerobic conditions, it was conducive to glycolysis (Levine and Puzio-Kuter, 2010; Wang et al., 2020a). According to reports, many glycolytic enzymes were upregulated in cancer, which was associated with poor prognosis. For example, HK2 (hexokinase-II) was a key metabolic enzyme in glycolysis pathway, the high expression of which was associated with poor prognosis of colorectal cancer and promoted glycolysis metabolism and cell proliferation (Shen et al., 2020). GLUT1 (glucose transporter 1) was a key factor involved in glucose uptake and metabolism, and its upregulation led to the transition of metabolism to aerobic glycolysis (Zhao et al., 2019). Other studies have shown that LDHA, as a glycolytic enzyme, plays a key role in aerobic glycolysis and is considered as an ideal target for tumor therapy (Pathria et al., 2018). Our study revealed that OCT1 upregulation promoted the expression of OCT1, HK2, GLUT1 and LDHA proteins
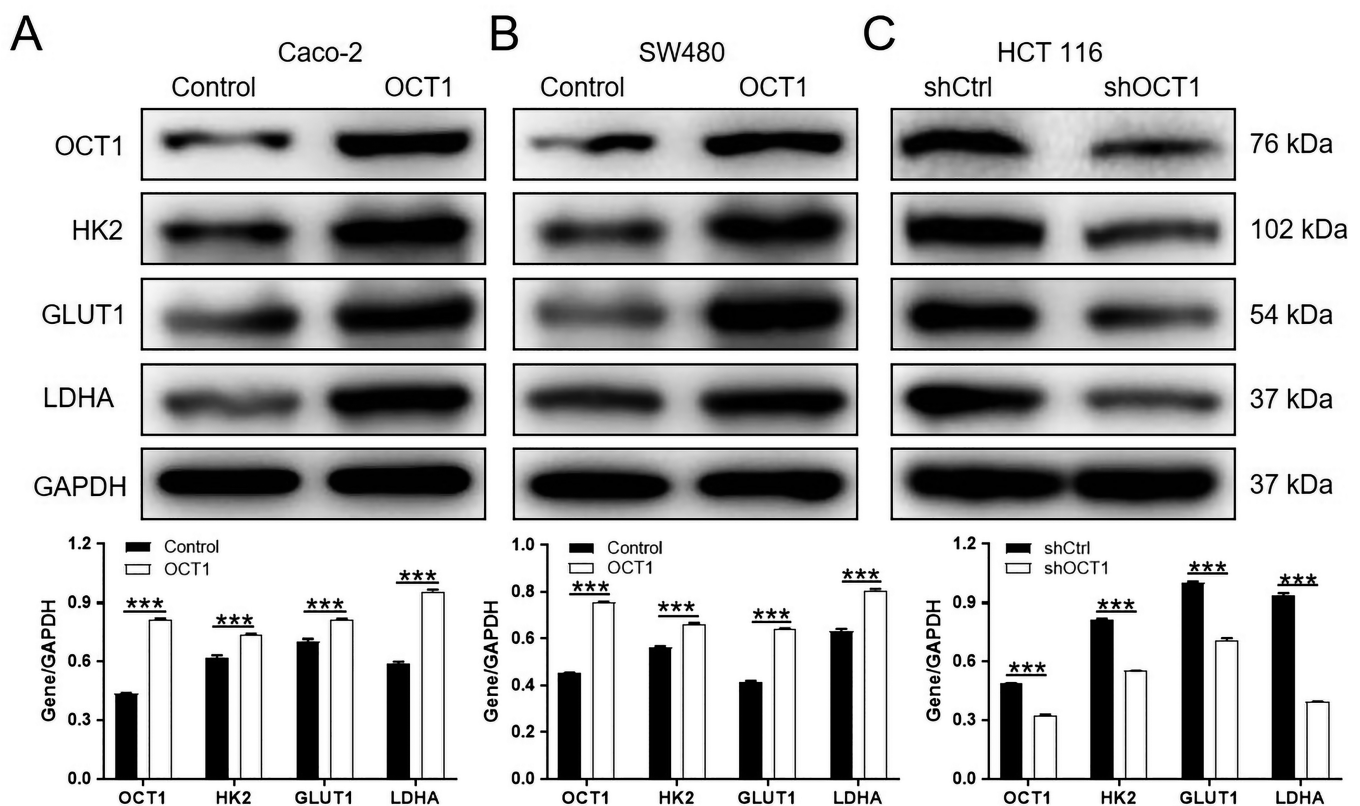

Fig. 6. OCT1 regulated the expression of LDHA protein and glycolytic associated proteins. **A-C.** Western blot was utilized for the detection of glycolytic associated protein expression in colorectal cancer cells after upregulated or downregulated OCT1, and the detection results were analyzed by gray scale. Control: Colorectal cancer cells infected with empty vector, as negative control; OCT1: colorectal cancer cells infected with OCT1 lentivirus for overexpressing OCT1 expression; shCtrl: colorectal cancer cells infected with empty vector, as negative control; shOCT1: colorectal cancer cells infected with shOCT1 lentivirus for downregulating OCT1 expression. *$P<0.05$; **$P<0.01$. ***$P<0.001$.

in Caco-2 and SW480 cells, while silencing OCT1 decreased the expression of OCT1 and HK2 proteins in HCT 116 cells. Therefore, we speculated that OCT1 may regulate glycolysis by acting on LDHA, and then play a role in the progression of colorectal cancer.

In summary, this study was based on the TCGA data in public database and found that OCT1 and LDHA were upregulated in colorectal cancer. Highly expressed OCT1 was associated with poor prognosis of patients with colorectal cancer, and promoted the migration of colorectal cancer cells. In addition, preliminary exploration of the mechanism of OCT1 found that OCT1 might promote glycolysis by regulating the expression of LDHA, suggesting that OCT1 played an important role in the migration and glycolysis of colorectal cancer cells. OCT1 and LDHA may be important targets for the treatment and prognosis of colorectal cancer.

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