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ZEB2-AS1 regulates the expression of TAB3 and promotes the development of colon cancer by adsorbing microRNA-188

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Abstract. – OBJECTIVE: This study aimed to explore the possible role and mechanism of lncRNA ZEB2-AS1 in the pathogenesis of colon cancer (CCa).

PATIENTS AND METHODS: The expression level of ZEB2-AS1 in 41 colon cancer tissue samples and 25 normal tissues was detected by qRT-PCR, and appropriate colon cancer cell lines were screened for *in vitro* experiments. Subcellular localization of ZEB2-AS1 was examined. After ZEB2-AS1 was transfected into colon cancer cells by liposome method, the cell proliferation, migration ability, and cell apoptosis percentage were evaluated by CCK-8 test, transwell assay, and flow cytometry, respectively. In addition, bioinformatics was applied to detect the target genes of microRNA-188. The Luciferase gene reporter assay was then performed to analyze the relative activity of Luciferase between microRNA-188 and TAB3 or ZEB2-AS1. At the same time, the control sequence, microRNA-188 mimics, microRNA-188 mimics+ ZEB2-AS1, si-TAB3, and microRNA-188 inhibitor+ si-TAB3 were respectively transfected into cells to further verify the interaction between TAB3 and microRNA-188 or ZEB2-AS1. Besides, the glucose and lactate levels were measured to explore their roles in glycolysis.

RESULTS: The expression of ZEB2-AS1 in colon cancer tissues and cells was significantly higher than that in normal ones, and ZEB2-AS1 was confirmed to be mostly located in the cytoplasm. In addition, ZEB2-AS1 overexpression could enhance the cell proliferation rate and migration ability as well as reduce the cell apoptosis, which could be reversed by microRNA-188 overexpression. In addition, bioinformatics prediction and Dual-Luciferase reporter assays revealed that ZEB2-AS1 could bind to microRNA-188, which could directly target TAB3. At the same time, it was found that the overexpression of ZEB2-AS1 and low expression of microRNA-188 promoted glycolysis, while the opposite result was observed after overexpression of microRNA-188 and low expression of TAB3.

CONCLUSIONS: The expression of ZEB2-AS1 is significantly increased in colon cancer tissues and cells, which can promote the proliferation, migration, and promote apoptosis of colon cancer cells. It may be involved in the development of this cancer through the process of glycolysis regulated by microRNA-188/TAB3.

Key Words:
Colon cancer, ZEB2-AS1, MicroRNA-188, TAB3, Glycolysis.

Introduction

Colon cancer is a common malignant digestive system tumor with high incidence and mortality worldwide. In China, colon cancer has become the third digestive tract tumor that causes death[1,2]. Surgery and chemoradiotherapy are still used to kill as many tumor cells as possible and reduce the number of tumor cells to achieve therapeutic effect. However, high recurrence and metastasis rates and high drug resistance rate make the 5-year survival rate after colon cancer still very low, which makes the study of early diagnosis and treatment of colon cancer particularly important. Therefore, it is of great practical significance and theoretical value to investigate the occurrence and development mechanisms of colon cancer at the molecular level[3-5].

Long non-coding RNAs (lncRNAs) are non-coding RNAs with a length of more than 200 nucleotides[6,7]. LncRNAs are widely distributed in the human body. The sequencing results of the whole human genome showed that less than 2% of the whole genome sequences were used to encode proteins, and most of the non-protein coding sequences were transcribed into lncRNAs with more than 200 bases. Although lncRNAs

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do not encode proteins, they participate in the formation of a complex and important regulatory network, thus subtly regulating gene expression. LncRNAs play an important role in normal tissue development, regulation of pluripotency and cell differentiation. In addition, they are involved in controlling cell proliferation, apoptosis, and cell migration. Therefore, the dysregulation of lncRNA expression is closely related to various diseases, including tumor formation[8,9]. Moreover, lncRNA regulates the expression of oncogenes and tumor suppressor genes at the epigenetic and transcriptional levels, participates in biological processes, such as cell proliferation, migration and invasion, and affects the occurrence and development of tumors. Therefore, lncRNAs are potential targets for the diagnosis, treatment, and prognosis of tumors.

ZEB2-AS1 is a natural antisense transcript of the 5'UTR of zinc finger e-box binding homologous box 2 (ZEB2), which is involved in the regulation of ZEB2 expression and may play a role in the progression of bladder cancer[10]. However, the role of ZEB2-AS1 in colon cancer has rarely been studied. In this study, we detected ZEB2-AS1 expression in colon cancer and explored its effect on the function of colon cancer cells, hoping to provide a new therapy target for this disease.

Patients and Methods

Sample Collection

The 41 colon cancer tissue specimens and adjacent normal ones were obtained from surgical specimens of patients treated in the First Affiliated Hospital of Zhengzhou University. None of the patients received chemotherapy or radiation therapy before surgery. Specimens were diagnosed by histopathology according to WTO standards, and tumor staging was performed according to the current TNM system. All specimens were quickly placed in liquid nitrogen for storage. All specimens obtained were reviewed by the Ethics Review Committee of The First Affiliated Hospital of the Zhengzhou University and approved by the patient or family member.

Cell Culture and Transfection

Normal colon cells (NCM460) and colon cancer cell lines (HCT116, LoVo, SW480, HT29) were purchased from American Type Culture Collection (ATCC, Manassas, VA, USA) and cultured in Dulbecco's Modified Eagle's Medium (DMEM; Thermo Fisher Scientific, Waltham, MA, USA) high glucose complete medium containing 10% fetal bovine serum (FBS) in a 37 °C, 5% CO2 incubator. Cells transfection was performed with Lipofectamine 2000 kit according to the instructions. The transfection sequences were as follows: si-TAB3, ZEB2-AS1 overexpression plasmid, microRNA-188 mimics and inhibitor, which were synthesized by Shanghai Jima company.

RNA Extraction and Quantitative Real Time-Polymerase Chain Reaction (qRT-PCR)

For both cell and tissue samples, the total RNA was extracted using TRIzol (Invitrogen, Carlsbad, CA, USA) reagent. The extracted RNA was transcribed into cDNA using the cDNA synthesis kit. The qRT-PCR was performed with the SYBR® Green Master Mix (TaKaRa, Otsu, Shiga, Japan). Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as an internal reference. The primer sequences were as follows: GAPDH (F: 5'-CACCCACTCCTCCACCTTTG-3', R: 5'-CCACCACCCTGTTGCTGTAG-3'), ZEB2-AS1 (F: 5'-GGCTGGATAGCAAAGGAC-3', R: 5'-ACACTCTTGGCGAGGT-3'); TAB3 (F: 5'-AGCAGCCCACAGCTTGATATT-3', R: 5'-ACTAGGAGAATGGATACCCAGGT-3'); PDK1(F: 5'-CTGTGATACGGATCAGAAACCG-3', R: 5'-TCCACCAAACAATAAAGAGTGCT-3'); PFK1 (F: 5'-GGTGCCCGTGTCTTCTTTGT-3', R: 5'-AAGCATCATCGAAACGCTCTC-3'); PKM2 (F: 5'-ATGTCGAAGCCCCATAGTGAA-3 ', R: 5'-TGGGTGGTGAATCAATGTCCA-3'). MiRNAs were detected using probes.

Nuclear Separation

The cells were digested and transferred to an Eppendorf (EP; Hamburg, Germany) tube, centrifuged for 5 min, and washed with phosphate-buffered saline (PBS). Then, a cell fractionation buffer was added into the cell pellets to lysis the cell fractions. After 10 min on ice, cells were centrifuged, and the upper supernatant was the cytoplasmic component while the nuclear component of the cell was located in the sediment. After the supernatant was transferred, the remaining pellets were added with the cell disruption buffer, mixed, and then allowed to stand on ice, which was the nuclear fraction. After lysis binding solution was separately added in the cytoplasmic and the nuclear fractions, anhydrous ethanol was added. The cells were centrifuged using an adsorption column, washed with a solution of 1, 2, 3, respectively, and finally eluted with an elution solution. The RNA concentration was measured,

and RNA was then reversely transcribed, which was followed by PCR detection.

Construction and Activity Detection of Luciferase Reporter Gene Vector

ZEB2-AS1 wild-type sequence (ZEB2-AS1 WT 3'UTR) and mutant sequence (ZEB2-AS1 MT 3'UTR) as well as TAB3 wild type sequence (TAB3 WT 3'UTR) and mutant sequence (TAB3 MT 3'UTR) were constructed. The cells were seeded in 96-well plates and 50 pmol/L microRNA-188-5p mimics or negative control was co-transfected with 80 ng of ZEB2-AS1 plasmid or TAB3 wild-type or mutant plasmid. After 48 h of transfection, the cells were lysed using a Dual-Luciferase reporter assay system to detect fluorescence intensity.

Cell Counting Kit (CCK-8) Assay

After transfection for 24 h, cells were digested and collected, and plated into 96-well plates at 2*103 per well, and 6 replicate wells were set in each group. After the cells were attached, the viability of the cells was determined by CCK-8 method. 2 h before the test, 10 μL of CCK-8 solution was added to each well, which were incubated at 37 °C for other 2 h. The absorbance of each well at 450 nm was measured using a microplate reader.

Cell Apoptosis

After transfection, the cells were added with 10 μL of Annexin V FITC fluorescent probe reagent. After gently mixed, 5 μL of propidium iodide (PI) dye was added to the mixture. Finally, 350 μL of binding buffer was added, and the suspension was gently mixed. After incubation at room temperature for 30 min in the dark, flow cytometry detection was performed.

Clonal Formation

Cells of each group in the logarithmic growth phase were gently washed with PBS and digested with 0.25% trypsin to prepare a cell suspension. A single cell suspension was prepared by diluting with a medium containing 10% fetal bovine serum (FBS). The cells were seeded in disposable culture dishes and cultured in a constant temperature incubator at 37 °C with 5% CO2, with 3 replicate wells per group. When macroscopic clones appeared in the culture dish (about 15 days after inoculation), the culture was terminated. After the removal of the culture medium, the cells were fixed with methanol, and stained with Giemsa for 10 min, and cell clones with a diameter larger than 50 μm were counted under a microscope.

Cell Migration

After transfection for 48 h, the cells were trypsinized and resuspended in serum-free medium. After cell counting, the diluted cell density was adjusted to 3.0×105/mL, and the transwell chamber containing Matrigel and no Matrigel was placed in a 24-well plate. 200 μL of the cell suspension was added in the upper chamber, and 500 μL of a medium containing 10% FBS was added to the lower chamber. After incubated in a 37 °C incubator for 48 hours, the chamber was removed, fixed with 4% paraformaldehyde for 30 min, and stained with crystal violet for 15 min. Subsequently, the cells were washed with PBS, and the inner surface of the basement membrane of the chamber was carefully cleaned to remove the inner layer cells. The perforated cells stained in the outer layer of the basement membrane of the chamber were observed under the microscope, and 5 fields of view were randomly selected.

Nude Mouse Tumor Formation Experiment

SW480 cells were digested and centrifuged at 300 rpm for 5 min at room temperature. Then, the supernatant was discarded, and cells were resuspended in 2 mL PBS and centrifuged again under the above conditions. After discarding the supernatant, the cells were washed with PBS and adjusted to a density of 1.5 *108/ml with an appropriate amount of PBS. Subsequently, the cells were inoculated into the loose connective tissue of the left lumbar and hip of the nude mouse with a micro-syringe, and the tumor nodules were visually observed at the inoculation site 1 week later. The maximum diameter a and the minimum diameter b of the tumor were measured on the 10th, 15th, 20th, 25th, and 30th day after subcutaneous injection of the cell stable strain using a Vernier caliper. The tumor volume was calculated according to the formula V = 1/2ab2, and the growth curve of the subcutaneous transplanted tumor in nude mice was drawn. This study was approved by the Animal Ethics Committee of the Zhengzhou University Animal Center.

Determination of Glucose and Lactic Acid Concentration

The cell supernatant was taken to determine the concentration of lactic acid by spectrophotometry. 2 mL of the cell culture medium was

collected, and the blank tube was added with distilled water, and the standard tube was added with 0.02 mL standard solution (3 mmol/L). Then, 1 mL of the enzyme working solution and the color developing agent were added to each tube. The spectrophotometer was zeroed with distilled water, and the absorbance values of the tubes were measured at 530 nm with a diameter of 1 cm, and the corresponding lactic acid concentration was calculated according to the standard curve. The glucose concentration was carried out according to the procedure using a Sigma-Aldrich (St. Louis, MO, USA) kit.

Statistical Analysis

The analysis was performed using SPSS 19.0 (SPSS IBM Corp., Armonk, NY, USA) statistical software. The measurement data were expressed as mean ± standard deviation, and the data between groups were compared by t-test. The difference was statistically significant at $p<0.05$. Correlation analysis was produced by GraphPad (La Jolla, CA, USA).

Results

ZEB2-AS1 Is Highly Expressed in Colon Cancer

We detected the expression of ZEB2-AS1 in normal colon cells (NCM460) and colon cancer cell lines (HCT116, LoVo, SW480, HT29) by real-time quantitative PCR, and found that the expression was significantly elevated in colon cancer cells, while the highest expression was observed in SW480 (Figure 1A), which was used for subsequent cell experiments. Meanwhile, the expression of ZEB2-AS1 in 41 colon cancer tissues and adjacent tissues was also detected by qRT-PCR. The results showed that the expression of ZEB2-AS1 in colon cancer tissues was significantly higher than that in adjacent tissues (Figure 1B). Moreover, ZEB2-AS1 expression was significantly higher in patients with stage III-IV tumors than patients with stage I-II tumors (Figure 1C). To further explore the mechanism of action of ZEB2-AS1, we performed cytoplasmic nuclear separation and detected the expression of cytoplasmic and nuclear ZEB2-AS1. The results showed that ZEB2-AS1 was mostly located in the cytoplasm (Figure 1D), indicating that it mainly participates in the occurrence of colon cancer at post-transcription level. Based on bioinformatics predictions of miRNAs that may bind to ZEB2-AS1, we found that microRNA-188 had the highest score. To explore the binding relationship between ZEB2-AS1 and microRNA-188, we designed a Dual-Luciferase reporter plasmid based on their binding sequence and performed the Dual-Luciferase assay (Figure 1E), which showed that microRNA-188 could reduce the Luciferase intensity in the ZEB2 -AS1 WT 3'UTR group, while no significant difference was observed in the ZEB2-AS1 MUT 3'UTR group, suggesting that ZEB2-AS1 can bind to microRNA-188 (Figure 1F). Further overexpression of ZEB2-AS1 in the cells revealed a significant decrease in the expression of microRNA-188 (Figure 1G). After overexpression of microRNA-188, the expression of ZEB2-AS1 was also inhibited (Figure 1H). In addition, the expression of microRNA-188 was significantly decreased in colon cancer (Figure 1I), and the expression of microRNA-188 expression was significantly lower in patients with stage III-IV tumor than that in patients with stage I-II tumor (Figure 1J). Correlation analysis showed that the expression of miR-188 was negatively correlated with that of ZEB2-AS1 (Figure 1K). These results indicated that ZEB2-AS1 is highly expressed in colon cancer and is capable of modulating the expression of microRNA-188.

MicroRNA-188 Inhibits the Pro-Tumor Effect of ZEB2-AS1

To further validate the role of microRNA-188 in the involvement of ZEB2-AS1 in colon cancer, the cells were transfected with ZEB2-AS1 overexpression plasmid, microRNA-188 mimics, and ZEB2-AS1+microRNA-188 mimics, respectively. The expression of ZEB2-AS1 was detected by qRT-PCR and it was found that the overexpression of microRNA-188 reversed the significant increase in ZEB2-AS1 caused by the ZEB2-AS1 overexpression plasmid (Figure 2A). Detection of cell proliferation revealed that microRNA-188 reversed the promoted cell proliferation caused by ZEB2-AS1 overexpression (Figure 2B). The results of clonal formation were consistent with those of the cell proliferation (Figure 2C), while flow cytometry assays showed that ZEB2-AS1 could inhibit cell apoptosis, while the overexpression of microRNA-188 promoted cell apoptosis (Figure 2D). To test the migration ability of colon cancer cells, we performed transwell experiments and found that high expression of ZEB2-AS1 significant-

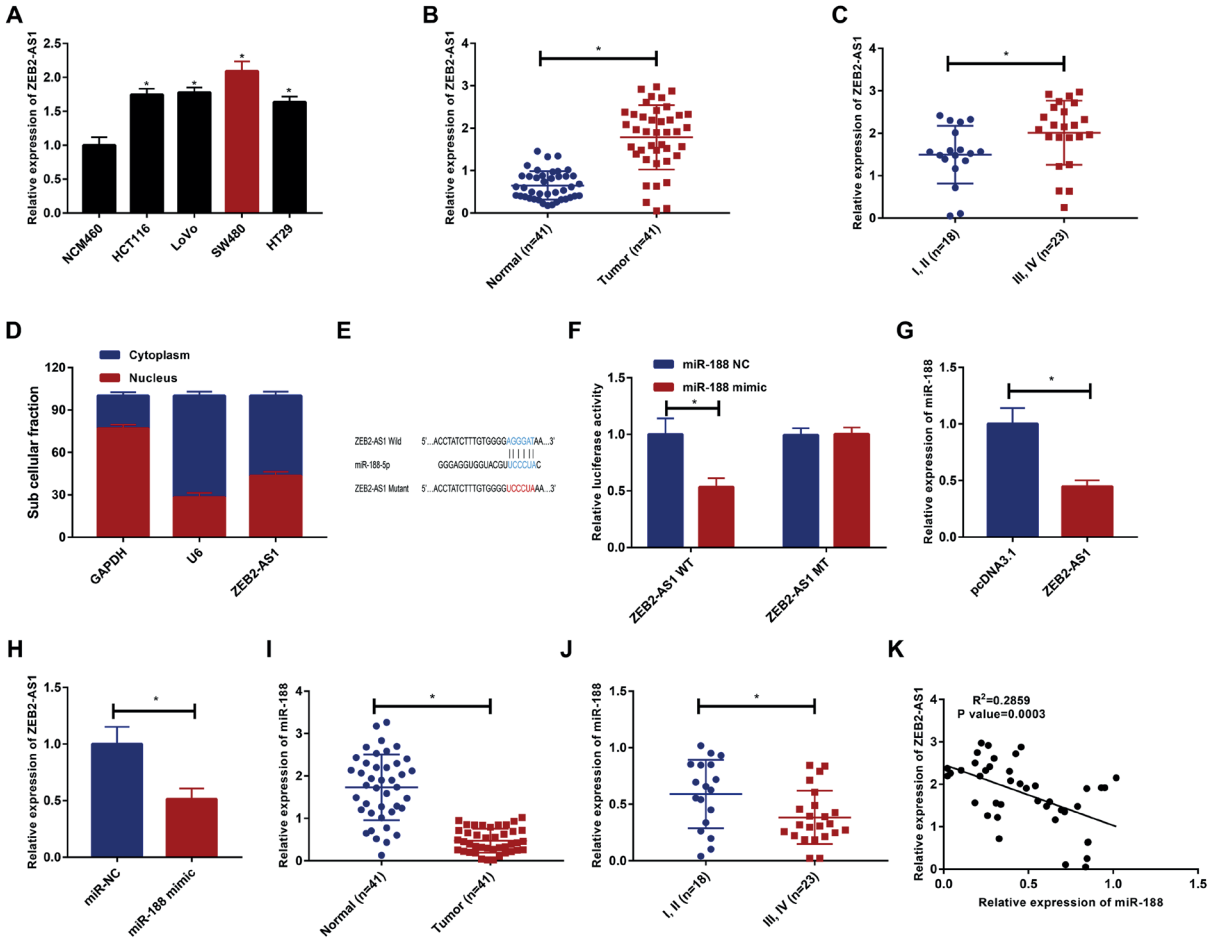

Figure 1. ZEB2-AS1 is highly expressed in colon cancer. **A,** Detection of ZEB2-AS1 expression in colon cancer cell lines by qRT-PCR. **B,** Detection of ZEB2-AS1 expression in colon cancer tissues by qRT-PCR. C, High expression of ZEB2-AS1 is positively correlated with tumor stage. **D,** Expression of ZEB2-AS1 in SW480 cells. **E,** ZEB2-AS1 and miR-188 binding sites were verified by Dual-Luciferase assay. **F,** miR-188 reduces the fluorescence intensity of ZEB2-AS1 wild-type reporter gene. **G,** Overexpression of ZEB2-AS1 inhibits miR-188 expression. H, overexpression of miR-188 inhibits ZEB2-AS1**. I,** Detection of miR-188 expression in colon cancer tissues by qRT-PCR. J, High expression of miR-188 is negatively correlated with tumor stage. **K,** ZEB2-AS1 and miR-188 are negatively correlated in colon cancer.

ly promoted the cell migration, while overexpressed microRNA-188 also reversed this effect (Figure 2E). In vivo, we injected colon cancer cells stably overexpressing ZEB2-AS1 into nude mice, and measured tumor diameters on 10, 15, 20, 25, and 30 days and plotted growth curves. The results showed that overexpressed ZEB2-AS1 could accelerate the tumor growth (Figure 2F). Meanwhile, the tumor weight was also significantly exacerbated in the ZEB2-AS1 group (Figure 2G). We detected the expression of microRNA-188 in the tumors and found a significant decrease (Figure 2H). These results further demonstrated that microRNA-188 may inhibit the pro-tumor effect of ZEB2-AS1.

TAB3 Is a MicroRNA-188 Target Gene

The role of miRNA is usually to degrade the target gene by binding to the 3'-UTR region of the target gene. Therefore, we predicted that the target gene that may bind to microRNA-188, and finally obtained TAB3 according to its function and score and constructed Dual-Fluorescein according to the binding sequence. The Dual-Luciferase reporter gene assay was used to detect the fluorescence intensity after transfection of TAB3 wild-type and mutant plasmids, as well as microRNA-188 mimics on SW480 cells (Figure 3A). The results showed that microRNA-188 could bind to TAB3 (Figure 3B). In addition, overexpression of microRNA-188 could significantly re-

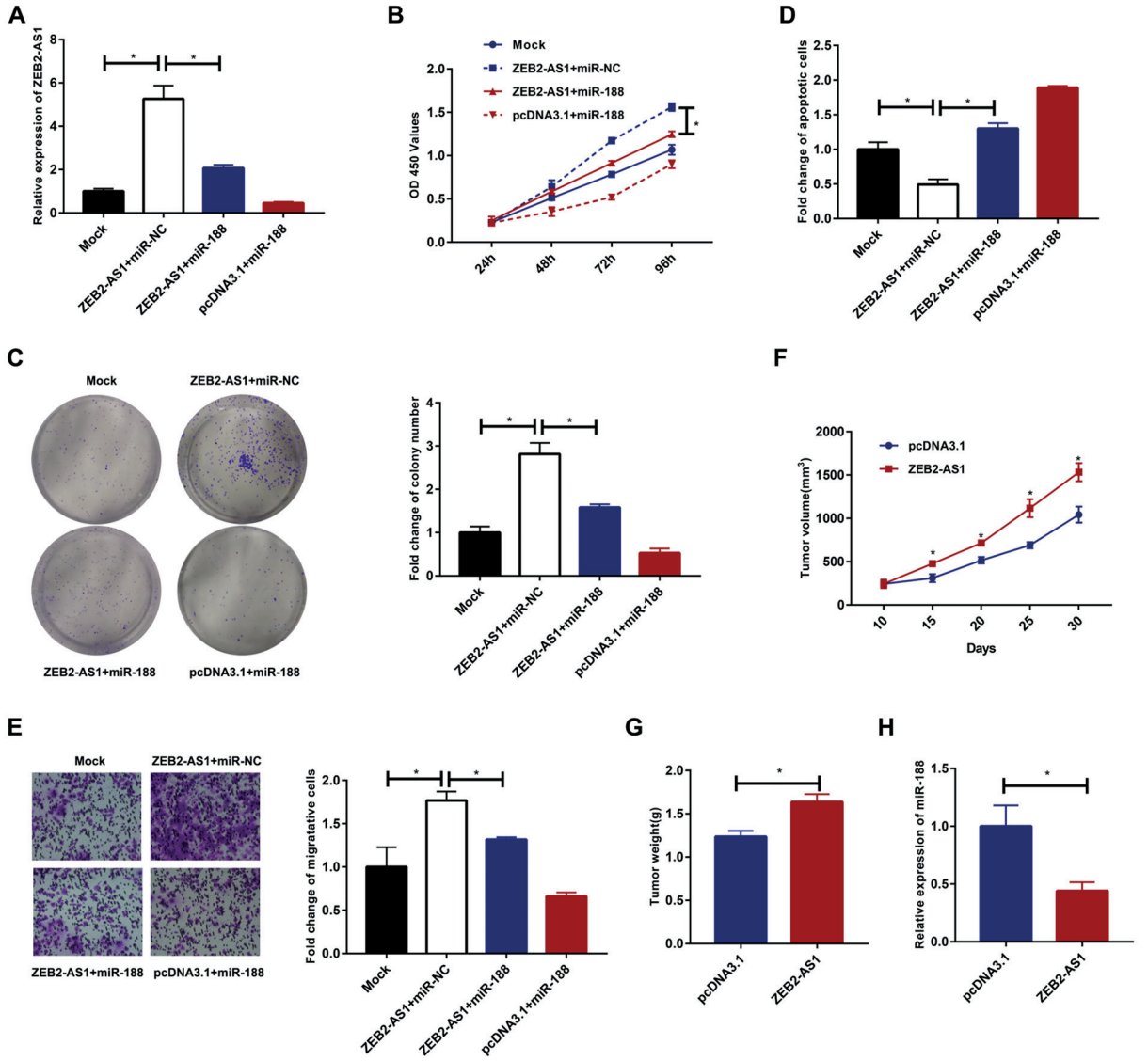

Figure 2. miR-188 inhibits the pro-tumor effect of ZEB2-AS1. **A,** Detection of miR-188 expression after co-transfection of miR-188 mimic and ZEB2-AS1 in SW480 cells. **B,** Cell proliferation was detected by CCK-8 assay after co-transfection of miR-188 mimic and ZEB2-AS1. **C,** Cell proliferation was detected by colony formation assay after co-transfection of miR-188 mimic and ZEB2-AS1 (10x). **D,** Detection of apoptosis after co-transfection of miR-188 mimic and ZEB2-AS1 by flow cytometry. **E,** Cell migration was detected by transwell assay after co-transfection of miR-188 mimic and ZEB2-AS1 (40x). **F,** Overexpression of ZEB2-AS1 promotes tumor volume in vivo. **G,** Overexpression of ZEB2-AS1 increases tumor weight in vivo. **H,** Overexpression of ZEB2-AS1 inhibits the expression of miR-188 in tumors *in vivo*.

duce the expression of TAB3 (Figure 3C), while microRNA-188 inhibition could significantly increase the expression of TAB3 after TAB3 silencing (Figure 3D). CCK-8, clone formation, apoptosis, and cell migration analysis revealed that low expression of microRNA-188 promoted cell proliferation and migration and inhibited cell apoptosis, while TAB3 knockdown could reverse the promoted tumorigenesis caused by low expression of microRNA-188 (Figure 3E-3H). These results further proved that TAB3 is the target gene of microRNA-188.

ZEB2-AS1 Regulates Cell Metabolism

Previous studies suggest that TAB3 can regulate the glycolysis of tumor cells. We wondered whether ZEB2-AS1 participated in colon cancer by regulating cell metabolism. The results indicated that overexpressed ZEB2-AS1 increased glucose and lactate production, while microR-

NA-188 overexpression inhibited the production of glucose and lactic acid, and the simultaneous treatment of ZEB2-AS1 and microRNA-188 could maintain the glucose and lactic acid in the intermediate state (Figure 4A-4C). Similarly, the low expression of microRNA-188 promoted the production of glucose and lactic acid, while the low expression of TAB3 reversed this effect (Figure 4D-4F). Next, we detected the expression of several major enzymes (PDK1, PFK1, and PKM2) and found that the overexpression of ZEB2-AS1 and the low expression of microRNA-188 promoted glycolysis, while the overexpression of microRNA-188 and the low expression of TAB3 inhibited glycolysis (Figure 4G-4I). These results indicated that ZEB2-AS1/microRNA-188/TAB3 may together regulate cellular metabolism.

Discussion

Colon cancer is a common malignant digestive system tumor with high morbidity and mortality. The susceptibility of colon cancer cells to invasion and metastasis is an important reason for the poor prognosis of colon cancer[11]. However, the

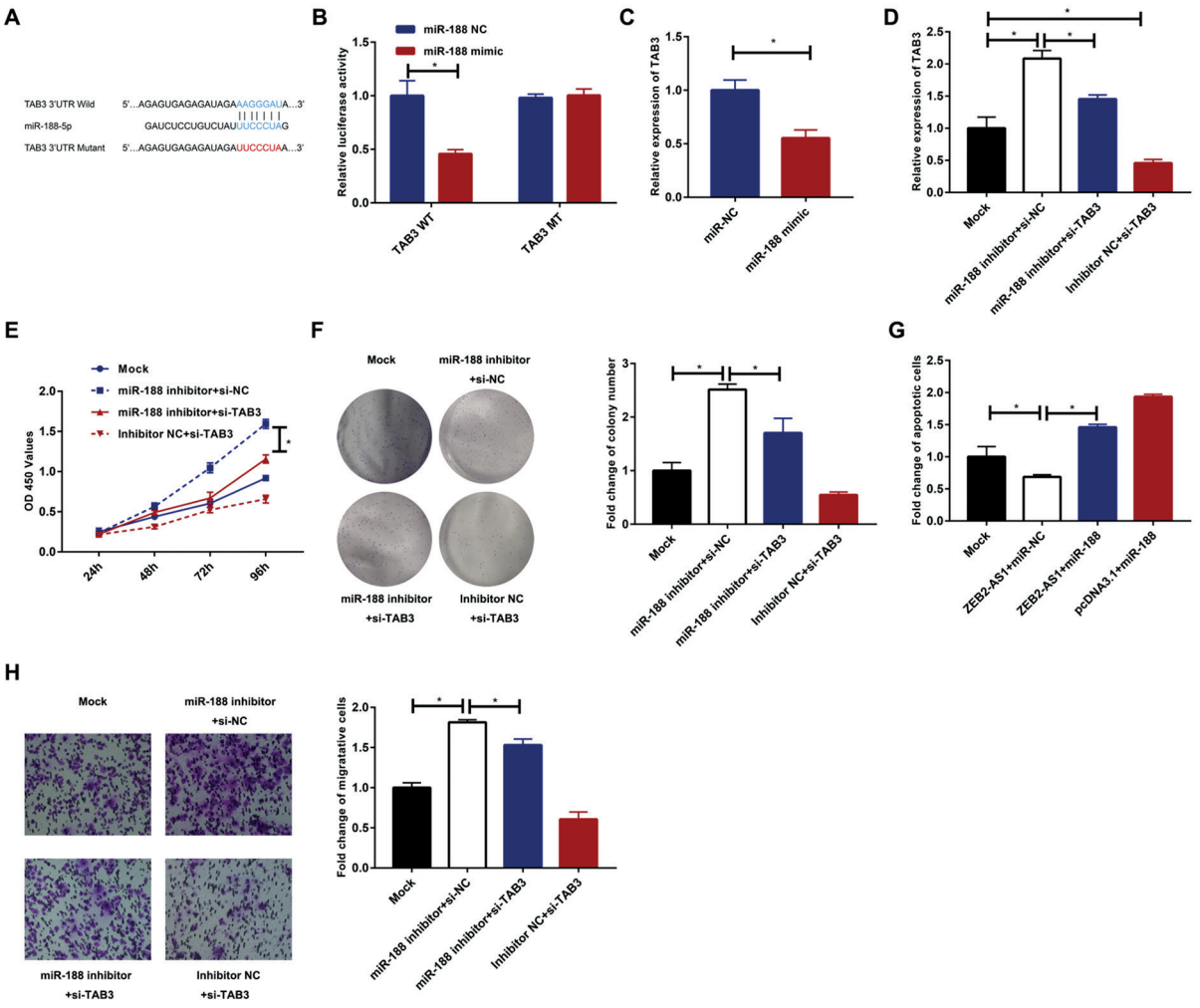

Figure 3. TAB3 is a miR-188 target gene. **A,** TAB3 and miR-188 binding sites are validated by Dual-Luciferase assay. **B,** miR-188 reduces the fluorescence intensity of TAB3 wild-type reporter gene. **C,** Overexpression of miR-188 inhibits TAB3 expression. **D,** TAB3 expression was detected by qRT-PCR after co-transfection of miR-188 inhibitor and si-TAB3. **E,** Cell proliferation was detected by CCK-8 assay after co-transfection of miR-188 inhibitor and si-TAB3. **F,** Cell proliferation was detected by colony formation assay after co-transfection of miR-188 inhibitor and si-TAB3 (10x). **G,** Detection of apoptosis after co-transfection of miR-188 inhibitor and si-TAB3 by flow cytometry. **H,** Cell migration was detected by transwell assay after co-transfection of miR-188 inhibitor and si-TAB3 (40x).

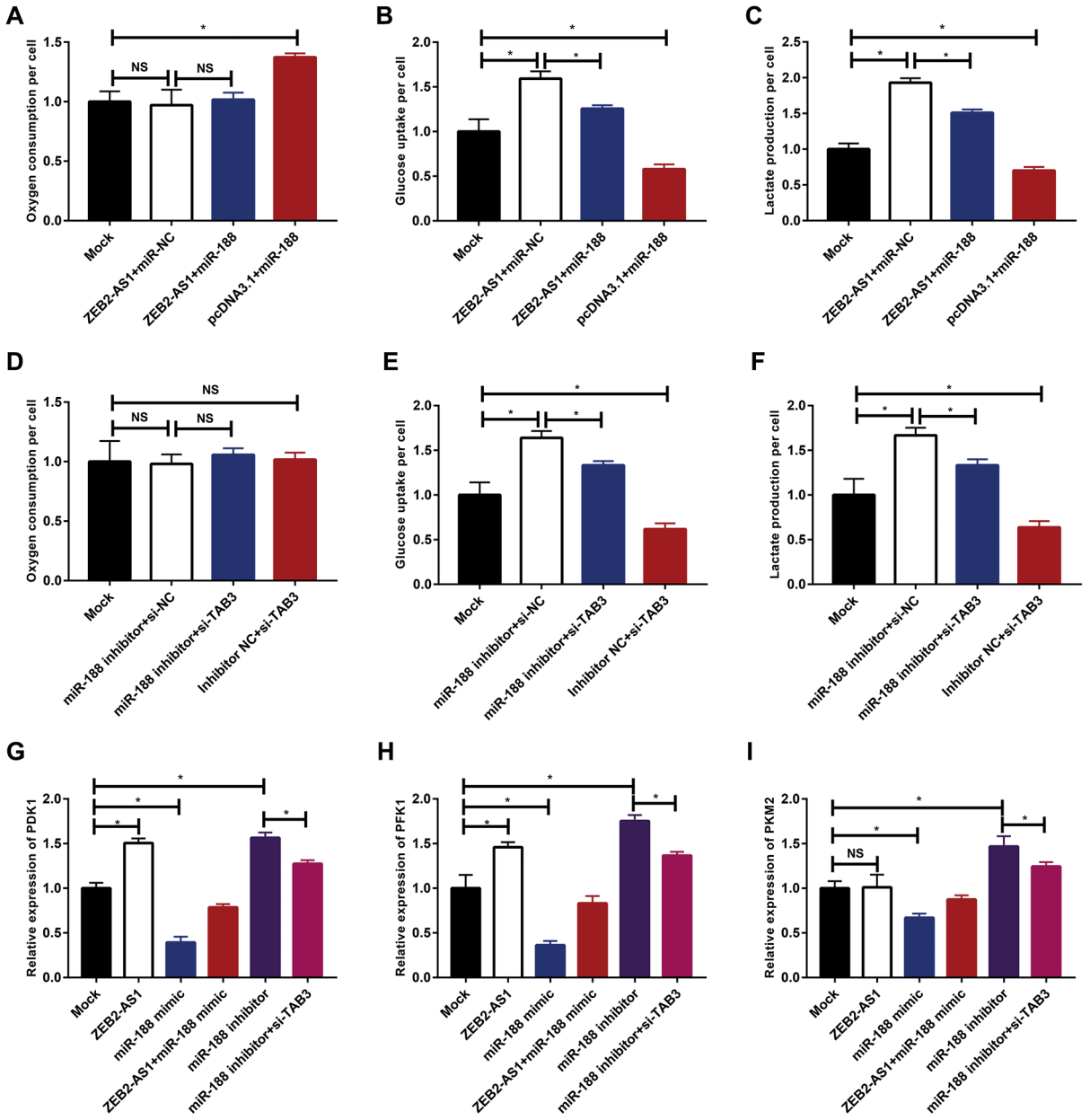

Figure 4. ZEB2-AS1 regulates cell metabolism. **A,** Overexpression of miR-188 promotes cellular oxygen uptake. **B-C**, overexpression of miR-188 inhibits ZEB2-AS1 promoting glucose uptake and lactate production. **D,** Low expression of TAB3 does not affect cellular oxygen uptake. **E-F,** Low expression of ZEB2-AS1 inhibits the expression of miR-188 and promotes glucose uptake and lactate production. **G-I,** detection of PDK1, PFK1 and PKM2 expression levels by qRT-PCR. NS, no significance.

specific mechanisms of inducing and promoting the invasion and metastasis of colon cancer cells have not been fully understood. The lack of tumor markers for early diagnosis and prediction of metastasis leads to many important challenges in the treatment of colon cancer. However, with the rapid development of modern cell and molecular biology, people begin to study the mechanisms of tumor occurrence and development from the molecular level, thus giving birth to the concept of tumor molecular targeted therapy, and the research in these fields has been highly concerned[12,13]. Therefore, in-depth exploration of the molecular mechanism of action in the occurrence and development of colon cancer and finding out the characteristic molecules related to anti-tumor

targets can provide a new method for the clinical prevention and treatment of colon cancer.

With the continuous discovery of lncRNAs, researchers[14,15] have paid more attention to the functions of lncRNAs in various biological processes and diseases. LncRNAs are competing endogenous RNAs (ceRNAs) containing miRNA response elements (MERs), which can inhibit the regulation of miRNAs on downstream genes by competitively binding miRNA sites. Although the expression abundance of lncRNAs in tumor cells is low, the expression level of lncRNAs is significantly changed[16,17], showing cell and tissue specificity and heterogeneity at different stages of tissue differentiation, which may be closely related to many biological processes. ZEB2-AS1 is a natural antisense transcript of the 5'UTR of zinc finger e-box binding homologous box 2 (ZEB2), which is involved in the regulation of ZEB2 expression and may play a role in the progression of bladder cancer[10]. Lan et al[18] discovered that low expression of ZEB2-AS1 in liver cancer inhibits tumor development. In pancreatic cancer, ZEB2-AS1 is involved in tumor development through miR-204/HMGB1[19]. Besides, ZEB2-AS1 regulates cell proliferation and invasion through the miR-143-5p/hif-1 alpha axis in gastric cancer[20-22]. However, the role of ZEB2-AS1 in colon cancer has rarely been observed. In this study, we found that the expression of ZEB2-AS1 was significantly increased in colon cancer, and it could regulate the formation of colon cancer through the microRNA-188/TAB3 axis.

As the seventh biological feature of tumor cells, aerobic glycolysis is attracting more attention. Glycolysis can not only rapidly provide sufficient energy for tumor cells, but also provide a large amount of raw materials for biosynthesis for the rapid proliferation of tumor cells[23,24]. Therefore, metabolic enzymes that determine the level of glycolysis play an important role in tumor development. PKM2 is highly expressed in gastric cancer and colon cancer tissues, promoting the rapid proliferation and migration of tumor cells[25]. PDK1 promotes proliferation and migration of NSCLC cells by enhancing the Warburg effect[26]. Of course, PFK1 protein, one of the three non-reactive catalytic enzymes in the glycolysis pathway, also plays an important role in the occurrence and development of tumors[27]. In this study, we found that the overexpression of ZEB2-AS1 and the low expression of microRNA-188 promoted glycolysis, while the overexpression of microRNA-188 and the low expression of TAB3 inhibited glycolysis.

Conclusions

In brief, these results revealed that ZEB2-AS1 is significantly increased in colon cancer, and the increased expression of ZEB2-AS1 promotes the proliferation, migration, and apoptosis of colon cancer cells through the regulation of glycolysis by microRNA-188/TAB3.

Conflict of Interests

The Authors declare that they have no conflict of interests.

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