Article

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METTL3 Regulates the Translation of Oncogene Myc through m^{6}A Modification and Promotes the Occurrence and Development of Cervical Cancer

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Background: Cervical cancer (CC) is one of the major types of gynecological cancer, with a high global incidence and mortality rate. Methyltransferase-like 3 (METTL3), a key constituent of methyltransferase, plays a crucial role in various biological processes. Still, only a rare report has been made on its involvement in the progression of CC. Therefore, this study aims to investigate the impact of METTL3 in CC and its molecular mechanisms.

Methods: Gene expression datasets about CC were obtained from the Gene Expression Omnibus (GEO) database, and the expression of *METTL3* and *Myc* was analyzed. Cell viability was detected after *METTL3* knockdown in HeLa and SiHa cells, followed by cell counting Kit-8 (CCK-8) assays. The relative expression of *METTL3* and *Myc* was detected via real-time quantitative PCR (qPCR) assays, and the protein expression was determined using Western blot. Meanwhile, cell invasion and migration capabilities were assessed utilizing transwell assays, and cell proliferation was detected using the EdU experiment. Furthermore, RNA methylation immunoprecipitation-qPCR detection was performed to determine the expression of *Myc* after N^6-methyladenosine (m^{6}A) modification.

Results: Analysis of the GEO database indicated elevated expression of METTL3 and Myc in CC tissues. Patients with high METTL3 expression had shorter disease-free survival, and patients with high Myc expression had shorter overall survival. Following the knockdown of *METTL3*, there was a significant reduction in the viability, proliferation, invasion, and migration abilities of HeLa and SiHa cells. Besides, the expression of *METTL3* and *Myc* mRNAs and proteins was greatly reduced. The level of m^{6}A *Myc* decreased significantly after *METTL3* knockdown.

Conclusions: *METTL3* plays an important role in regulating cervical cancer cells. *METTL3* promotes CC development through m^{6}A modification to regulate the expression of the oncogene *Myc*.

Keywords: METTL3; m^{6}A; Myc; cervical cancer

Introduction

As an important public health issue worldwide, cancer presents a grave menace to human well-being [1]. Cervical cancer (CC), as one of the major types of gynecological cancer [2], has a high global incidence and mortality rate, with an estimated 604,127 newly diagnosed CC cases worldwide in 2020 and an estimated 341,831 deaths [3]. Risk factors encompass tobacco use, alcohol consumption, oxidative stress-induced destructive free radicals, endogenous antioxidant defense system deficiencies, and infection with human papillomavirus (HPV) [4]. HPV is one of the key factors responsible for CC development [5]. Patients infected with the low-risk type often result in non-obvious infections or benign masses [6]. Conversely, high-risk HPV is associated with a propensity for viral-mediated malignant progression of lesions [7]. Many human CC cell lines reportedly contribute to developing certain chemotherapy drugs and identifying anti-cancer capabilities, namely cell lines of HPV16-positive CaSki and SiHa cells and HPV18-positive HeLa cells [8]. This cancer poses a significant threat to human health, primarily attributed to dysregulated proliferation and metastasis of malignant cervical cells, leading to local invasion and distant dissemination. Hence, novel biomarkers can be discovered to develop more accurate, individualized treatment options and early CC detection, and prolong patients' survival with corresponding measures.

N^6-methyladenosine (m^{6}A) is a critical epigenetic modification found on the nitrogen of the sixth adenine within RNA molecules. This modification represents the most prevalent form of RNA modification in mammalian mRNA [9]. The m^{6}A modification is associated with the pathological process of cancer [10], especially in transforming cancer cells. m^{6}A affects the expression of oncogene and tumor suppressor by regulating transcription, thus affecting tumor production. The major en-

zymes associated with m^6A include methylase, demethylase, and binding proteins. Methylases methyltransferase-like 3/4/5/14/16 (METTL3/4/5/14/16), RNA-binding motif protein 15 (RBM15), wilms tumor 1-associated protein (WTAP), and CBL proto-oncogene like 1 gene (CBLL1) enable m^6A methylation modification of bases on mRNAs; demethylases FTO and ALKBH5 are involved in removing m^6A modification; binding proteins YTH N^6-methyladenosine RNA binding protein C1/2 (YTHDC1/2), YTHDF1/2/3, insulin like growth factor 2 mRNA binding protein 1 (IGF2BP1/2/3), fragile x messenger ribonucleoprotein 1 (fmr1), eukaryotic translation initiation factor 3 subunit a (eif3a), heterogeneous nuclear ribonucleoprotein C (hnRNPC), and heterogeneous nuclear ribonucleoprotein A2/B1 (hnRPA2B1) can identify and bind to m^6A modified RNAs [11–13], which in turn affects the transport, translation, and degradation of RNAs. These enzymes regulate the expression of specific target genes through multiple regulatory factors and a complex network of interactions that alter malignant biological behavior. Conducting comprehensive investigations into the role of m^6A methylation in the initiation and advancement of cancer enhances our comprehension of the underlying mechanisms by which m^6A modification impacts tumor proliferation, metastasis, and resistance to therapeutic interventions. Therefore, further research and exploration of the mechanism of m^6A methylation is of significance for cancer prevention and treatment.

METTL3, a protein that binds to S-adenosylmethionine (SAM), is considered the primary characteristic component of the m^6A methyltransferase complex [14], mediating the methylation process of RNA in the nucleus. In addition, METTL3 is important for several biological processes, such as cell proliferation [15], differentiation [16], and apoptosis [17]. Achour *et al*. [18] investigated the role of METTL3 in modulating breast cancer-associated alternative splicing (AS) programs, providing insight into the function of METTL3 and m^6A in breast cancer by regulating tumor-associated AS switches. Chen *et al*. [19] proposed that METTL3 is a promising target for treatment of colorectal cancer (CRC), and METTL3 facilitates CRC progression by activating m^6A-GLUT1-mTORC1 axis; Guo *et al*. [20] have reported that METTL3 contributes to the malignant progression of head and neck squamous cell carcinoma (HNSCC) by enhancing the m^6A methylation of *CDC25B* mRNA, which stabilizes the transcript and promotes its expression. While the involvement of METTL3 in tumorigenesis has been established in various cancer types, its precise mechanism in CC is inadequately investigated. Therefore, this study examined the expression of *METTL3* and its association with CC, aiming to elucidate the molecular mechanisms by which *METTL3* regulates CC.

Materials and Methods

HeLa and SiHa Cell Culture and Transfection

HeLa cells (CL-0101, Procell, Wuhan, China) and SiHa cells (CL-0210, Procell, Wuhan, China) were placed in a dish at 5×10^6/dish, and the DMEM medium was refreshed after 24 h culture. By comparing the obtained STR profiles with known reference databases, the accuracy and identity of the HeLa and SiHa cell lines used in our experiments were confirmed, along with the absence of mycoplasma contamination. si*METTL3* was designed and constructed by Chongqing Biomedicine Biotechnology Co., Ltd. (Chongqing, China). 10 µL si*METTL3* and control substances were dissolved in 490 µL OPTI-MEM (31985-062, Gibco, Shanghai, China), respectively, gently mixed and incubated at room temperature for 5 min. Another two EP tubes were added 30 µL of transfection reagent LentifusionNanofusion version2.0 (10668-006, Biomedicine, Chongqing, China) respectively, dissolved in 470 µL of OPTI-MEM (31985-062, Gibco, Shanghai, China), gently mixed, and left on standby. The mixture containing the transfection reagent was added to the tubes containing si*METTL3* and the control tubes, respectively, mixed thoroughly, added uniformly to the culture dish, and vibrated well using the cruciform method. The cells were cultured again with a fresh complete medium after 6 h and collected after 48 h. si*METTL3* (forward): 5′-UCUAACUCAGGAUCUGUAGCU-3′; si*METTL3* (reverse): 5′-CUACAGAUCCUGAGUUAGAGA-3′; negative control (NC) (forward): 5′-UUCUCCGAACGUGUCACGUTT-3′; NC (reverse): 5′-ACGUGACACGUUCGGAGAATT-3′.

Analysis of the Gene Expression Omnibus (GEO) Database Cervical Cancer Dataset

The GEO database was utilized to search for CC data. Two datasets, namely GSE67522 and GSE30760, were obtained and examined to analyze the expression of *METTL3* and *Myc*. Survival analysis was conducted using the gene expression profile interactive analysis website, and corresponding Kaplan-Meier curves were generated.

CCK-8 Assay for HeLa and SiHa Cell Viability

After grouping, samples were added with 10 µL of cell counting Kit-8 (CCK-8) solution (C0038, Beyotime, Shanghai, China). Zero well without adding sample cells was set using corresponding culture solutions and CCK-8 solution. Following incubation of 1 h, absorbance was measured at 450 nm using a microplate reader (CMax Plus, Molecular Devices, MD, USA, USA).

Real-Time Quantitative PCR (QPCR)

RNA extraction of HeLa and SiHa cells was carried out employing Trizol reagent (15596-018, Thermo Fisher Scientific, Waltham, MA, USA) and cDNA synthesis using

Goldenstar™ RT6 cDNA Synthesis Kit Ver.2 (TSK302M, Tsingke, Beijing, China). The qPCR reaction system was prepared with reference to the instruction of 2 × T5 Fast qPCR Mix kit (SYBR Green I) (TSE002, Tsingke, Beijing, China) and then reacted using the fluorescence quantitative PCR instrument (IQ5, Bio-Rad, Hercules, CA, USA). Housekeep gene glyceraldehyde-3-phosphate dehydrogenase (*GAPDH*) was normalized, and its relative expression was calculated using the $2^{-\Delta\Delta Ct}$ method. Primers used were listed as following: *METTL3* (forward): 5′-AACTGCAACGCATCATTCGG-3′, *METTL3* (reverse): 5′-ATCCAGACCCTGGTTGAAGC-3′; *Myc* (forward): 5′-TAGTGGAAAACCAGCAGCCT-3′, *Myc* (reverse): 5′-TTCTCCTCCTCGTCGCAGTA-3′; *GAPDH* (forward): 5′-TCAAGGCTGAGAACGGGAAG-3′, *GAPDH* (reverse): 5′-TCGCCCCACTTGATTTTGGA-3′.

Western Blot

We extracted the total proteins of HeLa and SiHa cells, and their concentration was measured using the cytometric bead array (CBA) method. Following the quantification of protein concentration, 500 µg of protein was mixed with 5 × SDS Loading Buffer (4:1) and denatured by heating in a metal bath at 100 °C for 6 min to ensure complete denaturation of the proteins. 20 µL of each protein sample was applied for electrophoresis, then transferred to a membrane, sealed at room temperature with 5% skim milk for 1 h, and incubated at 4 °C overnight: METTL3 (1:1000, A19079, abclonal, Wuhan, China), Myc (1:1000, bs-8852R, Bioss antibodies, Beijing, China), and GAPDH (1:1000, A19056, abclonal, Wuhan, China). The following day, a secondary antibody (1:2000, AS014, abclonal, Wuhan, China) was used for incubation. The membrane was uniformly covered with enhanced chemiluminescence (ECL) exposure solution (34580, Thermo Fisher Scientific, Waltham, MA, USA) and determined in a nucleic acid protein gel imager (Universal Hood II, Bio-Rad, Hercules, CA, USA). The grayscale value of bands was measured using ImageJ (National Institutes of Health, Bethesda, MD, USA).

Transwell Detection of Cell Migration and Invasion

Migration ability: the cells were taken in good condition at 100% growth density. After removing the culture medium, sample cells went through PBS washing, with adding 0.25% pancreatin terminated digestion in time, centrifugation, and resuspension after another cycle of PBS washing to adjust at a density of 5 × 10^5/mL. In the transwell chamber, 100 µL of cell suspension was added to each well. After incubation at 37 °C under a 5% CO_2 condition, the cells were taken out, followed by two cycles of washing with calcium-free PBS, fixed with 4% paraformaldehyde, and added with 0.1% crystalline violet for staining. Unmigrated cells were wiped off using a wet cotton ball from the upper layer. After washing with PBS three times, the cells in random field view under a 100× microscope (CKX3-SLP, Olympus, Tokyo, Japan) were counted, and their average values were calculated.

Invasive ability: after serum-free medium and Matrigel (356234, Corning, Corning, NY, USA) were mixed in a 5:1 ratio, 100 µL was added to the transwell upper chamber for incubation at 37 °C. A "white layer" indicated the transformation into a solid state. After digestion termination and centrifugation, the culture solution was discarded. The cells were resuspended, and the density was adjusted to 5 × 10^5/mL. The solidified Matrigel was rinsed and then supplemented with 100 µL of cell suspension per well, and the lower chamber was supplemented with 500 µL of 20% FBS. After incubating at 37 °C in a 5% CO_2 incubator for 24 h, the cells were removed from the wells, which were rinsed twice using calcium-free PBS, followed by fixation with 4% paraformaldehyde for 20 min. Subsequently, crystal violet staining (1425163, Leagene, Beijing China) was performed for 20 min after PBS washing; the unmigrated cells were gently wiped off and washed with PBS three times. The cells at a random field view under the microscope were counted, and the average value was determined.

EdU Assay Detecting Cell Proliferation

After operation according to the BeyoClick™ EdU-488 Cell Proliferation Detection Kit (C0071S, Beyotime, Shanghai, China), the cells were observed in a fluorescence microscope (MF-53-LED, M-shot, Guangzhou, China).

RNA Methylation Immunoprecipitation-QPCR (MeRIP-QPCR)

The m^6A MeRIP kit (Bes5203, BersinBio, Guangzhou, China) was applied; the magnetic beads were coated using m^6A antibody (A19841, abclonal, Wuhan, China) or IgG antibody at room temperature; the supernatant was collected and added with an equal volume (200 µL) of phenol-chloroform-isoamyl alcohol mixture (25:24:1), and centrifuged at 13,000 ×g; the upper aqueous phase was collected, 1 µL of Glycogen, 20 µL of sodium acetate and 400 µL of 100% ethanol were added, fully inverted, mixed, let standby at –20 °C overnight for precipitation of RNA samples, and m^6A enrichment was assessed by qPCR.

Data Statistics and Analysis

R 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) was used for bioinformatics analysis, the R package GEOquery was used to download data from GEO, the limma package was used for differential analysis, and the ggplot package was used for visualization. Cell experiments were performed by GraphPad Prism 9.0 software (Dotmatics, Boston, MA, USA) for data statistics and drawing. An unpaired *t* test was used for comparison between groups, and $p < 0.05$ was considered statistically significant.

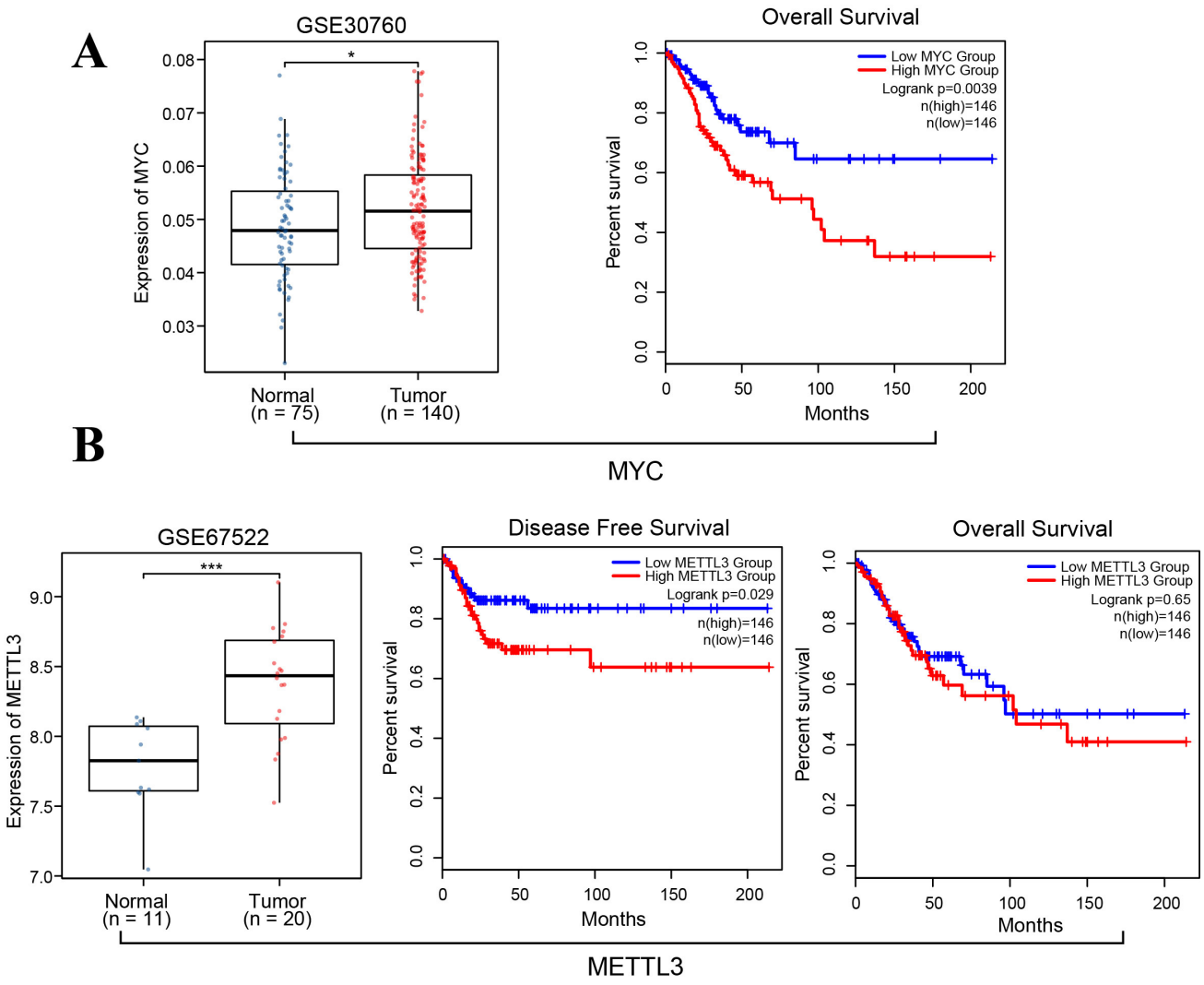

Fig. 1. Bioinformatic results of *Myc* and Methyltransferase-like 3 (METTL3) in cervical cancer (CC) tissues and their relationship with patients' life cycle. (A) *Myc* expression and prognosis in normal and CC tissues. (B) *METTL3* expression and prognosis in normal and CC tissues, * $p < 0.05$, *** $p < 0.001$.

Results

Myc and METTL3 are Overexpressed in CC Tissues

Bioinformatics analyses of the *Myc* level in the GSE30760 dataset revealed an apparent increase in CC tissues compared to normal cervical tissues ($p < 0.05$, Fig. 1A). Kaplan-Meier curve results implied that CC patients with a higher *Myc* level experienced shorter overall survival than those with a lower *Myc* level ($p = 0.0039$, Fig. 1A). Similarly, the expression profiling analysis of the extracted GEO database (GSE67522) demonstrated a notable overexpression of *METTL3* in CC tissues when compared to normal cervical tissues ($p < 0.001$, Fig. 1B). Therefore, CC patients observed at a high *METTL3* level tended to have significantly shorter disease-free survival than low-level subjects ($p = 0.029$, Fig. 1B). Still, no significant difference was revealed in overall survival ($p = 0.65$, Fig. 1B).

Decreased Viability and Myc Expression of HeLa and SiHa CC Cells after Down-Regulation of METTL3

To study the action mechanisms of *METTL3* in CC cells, HeLa and SiHa cells were selected as the research objects. After the knockdown of the *METTL3* gene, the silence effect was detected. The influence of *METTL3* on the viability of CC cells was evaluated using CCK-8 assays, which revealed a notable inhibition of HeLa and SiHa cell viability upon *METTL3* knockdown ($p < 0.05$, $p < 0.01$, Fig. 2A). Furthermore, *METTL3* and *Myc* expression in the knockdown group was significantly reduced ($p < 0.001$, Fig. 2B). Meanwhile, the expression of METTL3 and Myc in each experimental group was also detected using Western blot. The findings indicated a significant decrease in the expression of METTL3 and Myc proteins in HeLa and SiHa cells following the knockdown of *METTL3* ($p < 0.01$, $p < 0.001$, Fig. 2C), and *METTL3* was speculated to regulate the expression of *Myc*.

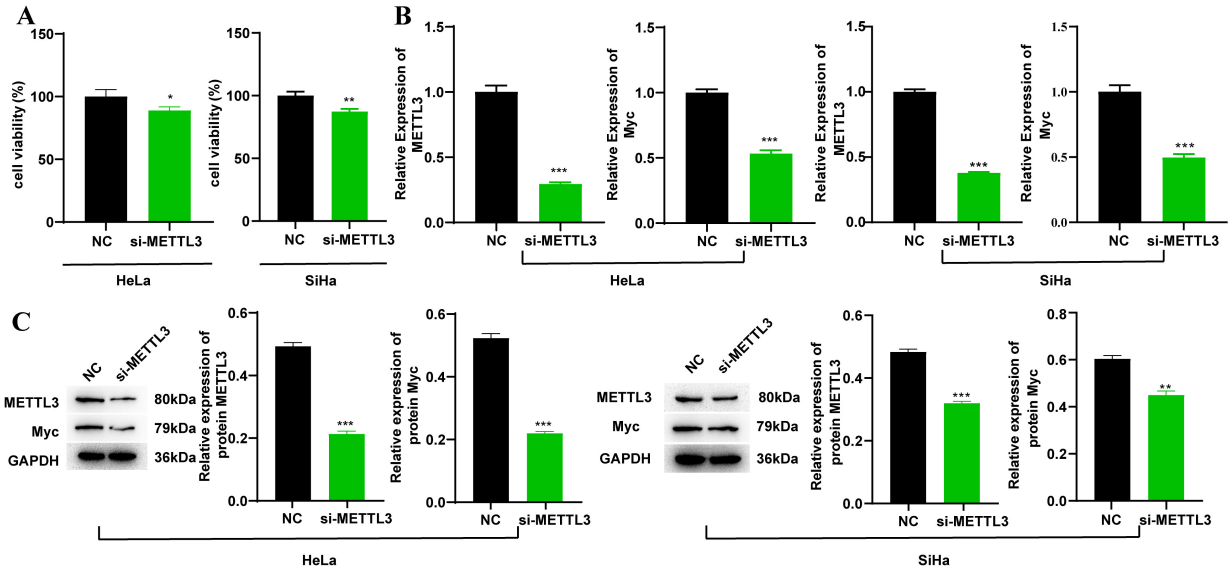

Fig. 2. Effect of knocking down *METTL3* on the proliferation activity, *METTL3*, and *Myc* expression of HeLa and SiHa cells. (A) Cell counting Kit-8 (CCK-8) detection of the proliferation of HeLa and SiHa cells after *METTL3* knockdown. (B) Real-time quantitative PCR (qPCR) detection of the relative expression of *METTL3* mRNA and *Myc* mRNA in HeLa and SiHa cells after knocking down *METTL3*. (C) Western blot detection of the expression of METTL3 and Myc in HeLa and SiHa cells after knocking down *METTL3*. Compared to empty load, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, n = 3. GAPDH, glyceraldehyde-3-phosphate dehydrogenase; NC, negative control.

Down-Regulation of METTL3 Inhibits Invasion and Migration of HeLa and SiHa Cells

Transwell experiments were performed to explore the effect of *METTL3* on the invasion and migration abilities of CC cells. The findings indicated a significant reduction in the invasion and migration of HeLa and SiHa CC cells following *METTL3* knockdown compared to the corresponding empty vector of the control group ($p < 0.01$, $p < 0.001$, Fig. 3A–D). It has been shown that the knockdown of *METTL3* substantially inhibited cell invasion and migration in CC tissues.

Knockdown of METTL3 Reduces CC Cell Proliferation and Regulates Expression of Myc by Identifying m^{6}A-Modified Myc

EdU experiment detected proliferation in HeLa and SiHa cells. In the *METTL3* interference group, the proliferation rate was reduced compared with the corresponding empty load group, and there was a significant difference ($p < 0.001$, Fig. 4A,B), suggesting that *METTL3* knockdown inhibited CC cell proliferation. The previous qPCR and Western blot results indicated an apparent reduction of *Myc* expression in HeLa and SiHa cells after *METTL3* knockdown (Fig. 2B,C). To gain further insights into whether METTL3 regulates Myc expression, a MeRIP-qPCR experiment was conducted. The results showed that after knocking down *METTL3*, the level of m^{6}A *Myc* decreased significantly (Fig. 4C), indicating that *METTL3* regulates *Myc* expression through m^{6}A modification.

Discussion

Standard treatment options for CC include surgery, chemotherapy, and radiotherapy. Although the clinical efficacy of CC has improved as treatment therapies advance, postoperative relapse and metastasis of CC cases are still high [21]. Currently, treatment measures for CC relapse or metastasis are limited. Patients diagnosed with CC often face a challenging prognosis, with median overall survival ranging from 7 to 53 months and a 5-year survival rate as low as 17% [22]. Therefore, exploring new therapeutic targets is of great significance in improving the treatment effect and prognosis of CC. Previous studies have shown that *METTL3* is involved in the occurrence of various cancers such as breast cancer, CRC and HNSCC [18–20], but its role in CC has not been fully studied. Therefore, the present study aimed to reveal the molecular mechanism of *METTL3* regulation in CC.

Numerous studies have provided evidence that aberrant alterations in m^{6}A modification can result in dysregulated expression of oncogenes and tumor suppressor genes, which may affect the development of CC, patient response to immunotherapy, and clinical prognosis. Among CC cases, the reduction of m^{6}A is closely related to tumor size, FIGO staging, degrees of differentiation, lymph node infiltration, and relapse [23], so m^{6}A mRNA methylation may be a potential therapeutic target for CC. METTL3, a prominent methyltransferase responsible for modulating m^{6}A levels, holds significant importance in various types of

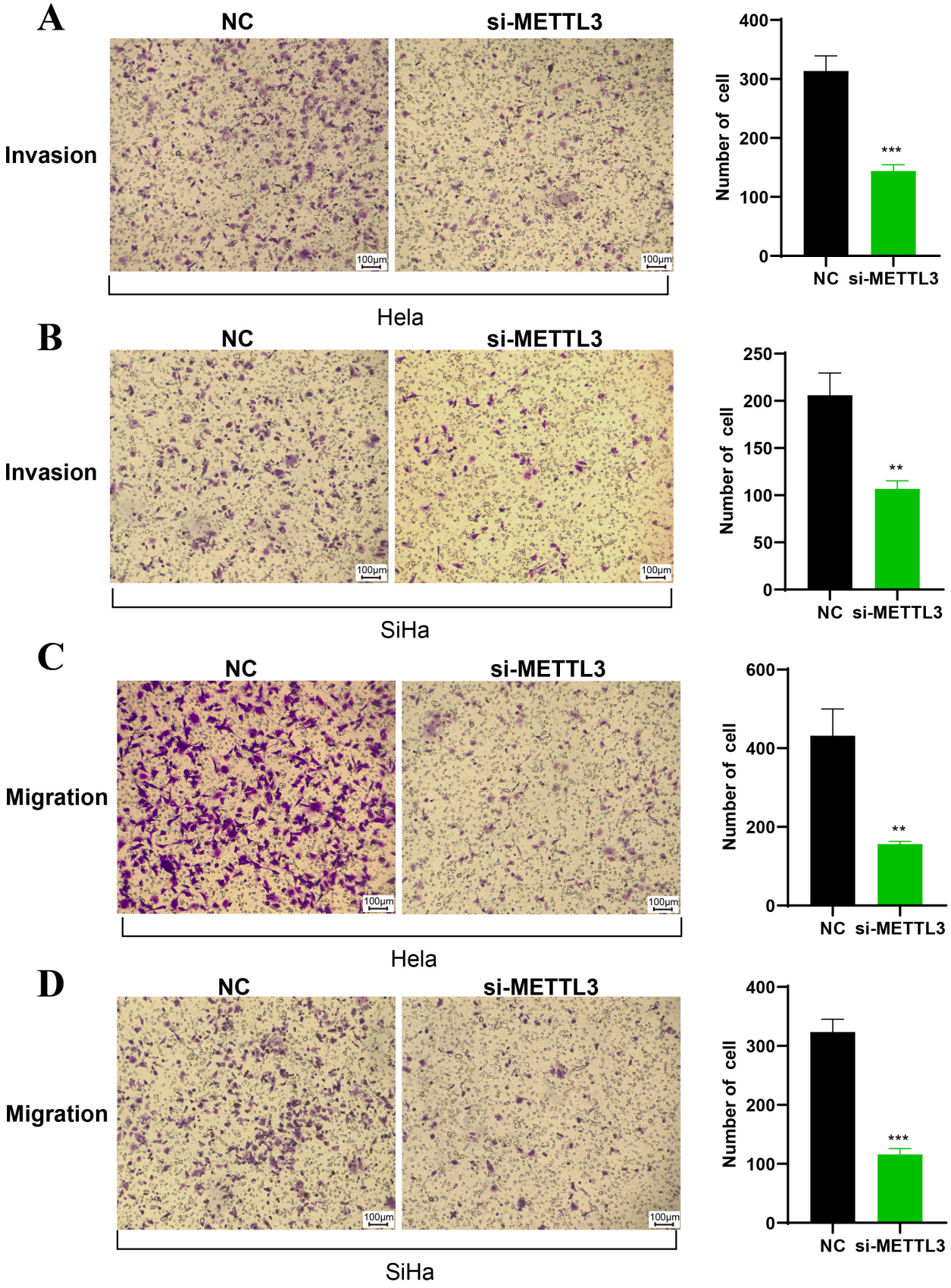

Fig. 3. Transwell experiment detection of the invasion and migration of HeLa and SiHa cells (100×). (A) HeLa cell invasion ability. (B) SiHa cell invasion ability. (C) HeLa and (D) SiHa cell migration abilities. Scale bar = 100 μm. Compared to empty load, ** $p <$ 0.01, *** $p < 0.001$, n = 3. NC, negative control.

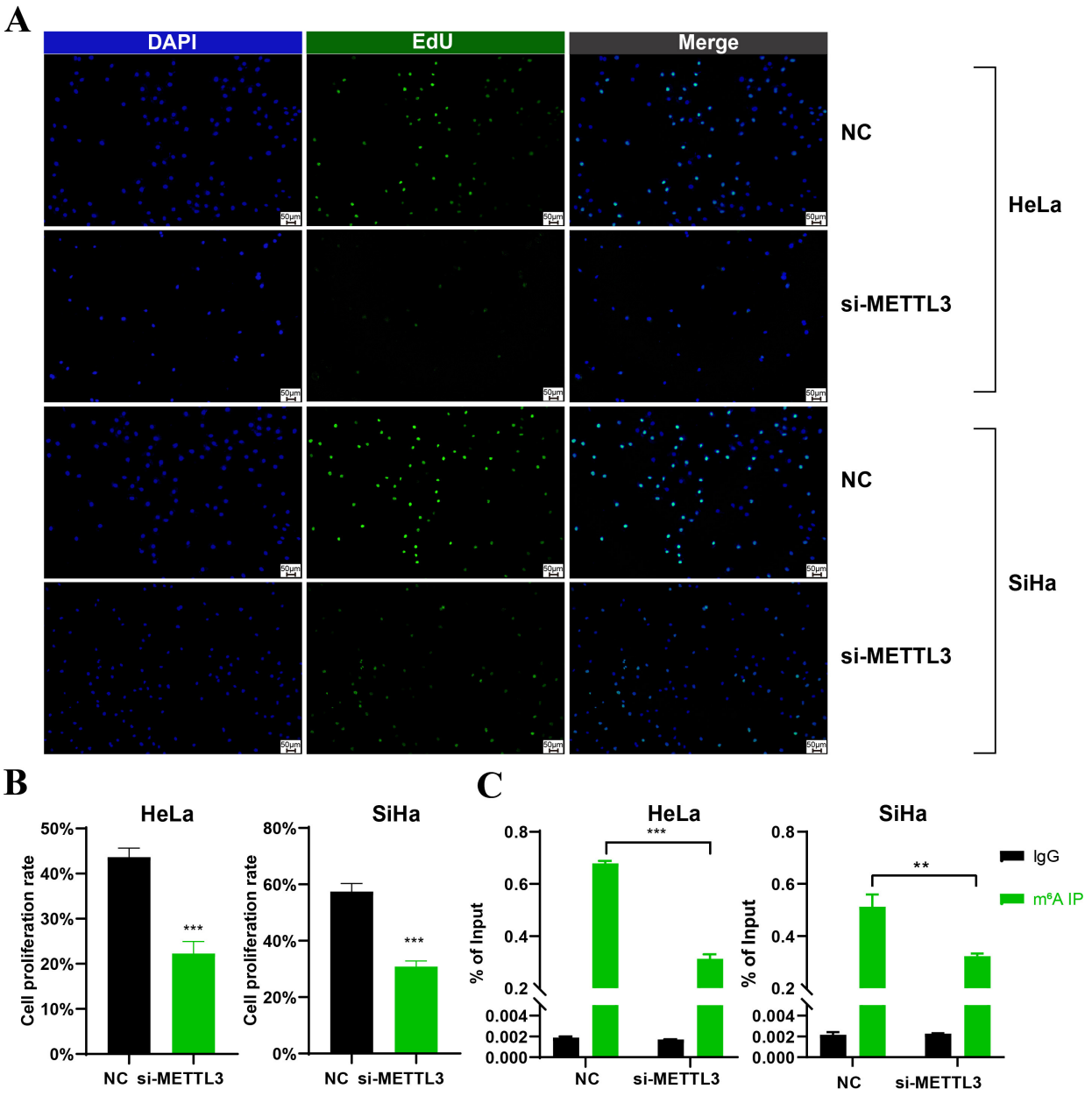

Fig. 4. Knockdown of *METTL3* inhibited the proliferation of HeLa and SiHa cells and regulated the expression of *Myc*. (A) The EdU experiment detection of the proliferation of cells in each group. Scale bar = 50 µm. (B) EdU experiment detection of HeLa and SiHa cell proliferation. (C) RNA methylation immunoprecipitation-qPCR (MeRIP-qPCR) detection of the way that *METTL3* regulates *Myc*, ** $p < 0.01$, *** $p < 0.001$, n = 3. m^6A, N^6-methyladenosine.

tumors. In hepatocellular carcinoma, for instance, *METTL3* increases growth-related *SOCS2* mRNA reduction through m^6A [24]. Meanwhile, *METTL3* boosts the growth of gastric cancer by increasing the mRNA stability of *HDGF* in an m^6A-dependent manner, thereby promoting cancer proliferation [25]. In CC, one study has found increased levels of *METTL3* expression [26]. By targeting the knockdown of m^6A methyltransferase (*METTL3* and *METTL14*) to downregulate m^6A, it promotes the proliferation of CC cells, while overexpression of *METTL3* and *METTL14* or knockdown of m^6A demethylase (FTO and ALKBH5) to regulate elevated m^6A levels, it suppresses CC cell proliferation [23]. Furthermore, elevated *METTL3* expression in CC has been found to enhance the stability of HK2 through YTHDF1-mediated m^6A modification. This process promotes the Warburg effect in CC, leading to lymph node metastasis and ultimately contributing to a poor prognosis [27]. *METTL3* reportedly regulates the maturation process of miR-193b in an m^6A-dependent manner, and reintroducing miR-193b *in vivo* and *in vitro* through cyclin D1 (CCND1) targeting can significantly inhibit the occurrence of CC [28]. At the same time, *METTL3* can also enhance

the stability of FOXD2-AS1 and maintain its expression; that is, METTL3/FOXD2-AS1 accelerates the progression of CC in an m^{6}A-dependent manner [29], indicating that *METTL3* might be a potential therapeutic target for CC. METTL3 was found to be highly expressed in CC through database comparison in the present study, suggesting that it might be related to the occurrence of CC. To further explore the mechanism of action of *METTL3*, this study uncovered that the viability, proliferation, migration, and invasion of CC cells after knockdown of *METTL3* were significantly reduced compared with the empty-load group, and the expression of *METTL3* and *Myc* mRNAs and proteins was greatly reduced, indicating that *METTL3* might be potential for CC treatment. These findings establish a theoretical foundation for further research and developing treatment strategies targeting *METTL3*.

Amplification of the *Myc* proto-oncogene is intricately linked to tumor initiation, progression, and metastasis. It exhibits high expression levels in various cancers, including CC, breast, and gastric [30]. Nevertheless, the precise mechanism by which it contributes to tumor initiation and progression remains incompletely elucidated. It is worth noting that *Myc* overexpression is frequently observed in human papillomavirus (HPV)–infected CC [31], located on chromosome site 8q24.21. Its overexpression is sometimes associated with the integration of HPV into the flanking area [32]. In HeLa cells positive for HPV18 infection, the HPV18 genome integrates into the chromosomal region 8q24.21, resulting in increased expression of the Myc protein [33]. Upregulation of *Myc* is prevalent in HPV-associated CC, which is consistent with the findings of this study via the database that *Myc* is overexpressed in CC cells. In addition, this study also revealed a substantial reduction of *Myc* mRNA and protein expression in HeLa and SiHa cells after *METTL3* knockdown, suggesting that *METTL3* may regulate the expression of *Myc*. The m^{6}A modification plays an important role in regulation [34], so we further explored the modulation of Myc expression by the m^{6}A modification. MeRIP-qPCR experiments demonstrated that METTL3 mediated Myc expression by modulating m^{6}A modification.

Although we have initially explored the role of METTL3 and Myc in regulating CC cells, it should be acknowledged that there are several limitations. Firstly, this study primarily focused on HeLa and SiHa cell lines, but further validation in animal models or patient samples is necessary to confirm the role of *METTL3* in CC progression. Secondly, while the study suggests that *METTL3* regulates *Myc* expression through m^{6}A modification, the exact molecular mechanisms underlying this regulation remain unclear. Further mechanistic studies are needed to elucidate the detailed pathways involved. In future studies, we will investigate the expression levels of *METTL3* and *Myc* in animal models or patient samples, which will help establish their clinical relevance and potential as prognostic markers. Furthermore, we will study the interaction network of METTL3 with other genes or proteins associated with CC to gain a more comprehensive understanding of METTL3's regulatory functions in disease progression.

Conclusions

METTL3 was essential for regulating the proliferation and migration of CC cells, and it might affect the expression of *Myc* by regulating m^{6}A modification and thus participate in the development and progression of CC. These findings provide us with evidence to facilitate a further understanding of the relationship between *METTL3* and *Myc* in CC development and progression. They also contribute to the research and development of new treatment strategies and targeted drugs with more effective options for CC patients. However, the specific mechanism still needs to be explored.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

YM and WZ designed the study. YM and HS performed the study, data analysis, and manuscript writing. WZ revised the manuscript. All authors contributed significantly to editorial changes of important content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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