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Original Article

Eukaryotic initiation factor 3b regulates the development and progression of breast cancer

Yanhui Li[1*], Jianhua Zhao[2*], Zhikun Yuan[3*], Dehan Yuan[4*], Mao Fang[5], Minru Xie[1], Minghan Xia[6]

[1]Department of Pathology, Shijie Hospital, Shijie Town, Dongguan, Guangdong, China; [2]Vice Principal's Office, Shijie Hospital, Shijie Town, Dongguan, Guangdong, China; [3]Department of Joint Surgery, Shijie Hospital, Shijie Town, Dongguan, Guangdong, China; [4]Department of General Surgery, Shijie Hospital, Shijie Town, Dongguan, Guangdong, China; [5]Department of Pathology, Guangzhou Medical University, Guangzhou, Guangdong, China; [6]Department of Pathology, The First Hospital of Jinan University, Guangzhou, Guangdong, China. [*]Equal contributors.

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Abstract: The tumorigenesis of breast cancer is a complex process involving multiple factors, among which abnormal gene expression is a key event. Nevertheless, studies on the regulation of gene expression have focused primarily on the transcriptional level, although the abnormal translation regulation is also closely related to tumorigenesis. Accumulating evidence has indicated the dysregulation of eukaryotic initiation factor (eIF) subunits in a variety of tumors, which contributes to the malignant transformation, tumor growth, metastasis, and the prognosis of patients. In this study, we examined the expression of eIF3b and found an upregulation of eIF3b in breast cancer cell lines as well as tumor tissues. In addition, the expression of eIF3b was related to the tumor stage with highest eIF3b expression in TNM stage III-IV and/or lymph node metastatic breast cancer. Furthermore, in vitro experiments demonstrated that eIF3b knockdown markedly inhibited tumor hyperplasia as well as the migration and invasion of breast cancer cells, while eIF3b overexpression showed the opposite effects. Importantly, eIF3b silencing inhibited the growth and pulmonary metastasis of xenograft tumor in breast cancer mouse model. Mechanistically, we found that eIF3b downregulation suppressed the malignant development of breast cancer by modulating Wnt/β-catenin pathway. Collectively, our data suggested that eIF3b might not only participate in the tumorigenesis of breast cancer, but also promote the proliferation, invasion, and metastasis of tumor cells. Thus, eIF3b may service as a potential therapeutic target for the treatment of patients with breast cancer.

Keywords: Breast cancer, eukaryotic initiation factor 3B, tumor growth, metastasis, invasion, Wnt/β-catenin pathway

Introduction

Epidemiological surveys have shown that the incidence of breast cancer accounts for about 15% of all malignancies in women. Breast cancer can be classified into different subtypes including ductal carcinoma, lobular carcinoma, and rare histological types of breast cancer (colloid carcinoma, medullary carcinoma, tubular carcinoma, inflammatory carcinoma). The prognosis of breast cancer varies greatly among patients, which may be related to the complex molecular mechanisms underlying the development of breast cancer. Numerous studies have demonstrated that protein synthesis is dysregulated during the malignant transformation and progression of breast cancer; however, the underlying mechanism remains unclear [1, 2]. Therefore, understanding the molecular events during tumorigenesis will provide important information for the prevention and intervention of breast cancer. Eukaryotic translation initiation factors (eIFs) are a superfamily of proteins that control the initiation of protein translation in eukaryotes as well as influence cell proliferation and malignant transformation. There are multiple core subunits of eIF3, among which eIF3b binds to RNA through its RNA recognition domain. eIF3b also has specific structure and scaffolding roles within the eIF3 complex. Importantly, silencing eIF3b inhibits tumor cell proliferation, while eIF3b upregulation can induce malignant tumor development. Indeed, in 2001, Lin et al. confirmed an abnormal

upregulation of eIF3b in human breast cancer [3], and Wang et al. demonstrated that eIF3b inhibition in vitro suppressed tumor cell growth, blocked cell cycle G1/S phase progression, and reduced tumor metastasis [4]. Similarly, Liang et al. showed that eIF3b expression was significantly increased in human glioblastoma tumors, and that eIF3b knockdown in the U87 cell line significantly arrested cells in G0/G1 phase and enhanced apoptosis [5], leading to the inhibition of U87 cell proliferation. Furthermore, Liang et al. have reported that eIF3b promotes cancer progression by modulating the β-catenin signaling pathway in esophageal squamous carcinoma [6]. Together, these data clearly demonstrate that eIF3b is important to the development and progression of tumors. Nevertheless, although there are some studies on the structure and function of eIF3b, the mechanisms by which eIF3b regulates breast cancer proliferation and invasion remain to be fully elucidated. Here, we studied the regulatory function of eIF3b in breast cancer cell proliferation and migration in vitro as well as in xenograft tumor growth in vivo.

Material and methods

Antibodies and reagents

A complementary DNA reverse transcription kit and RT-PCR kits were purchased from Invitrogen, USA. FBS, RPMI-1640 cell culture medium, and Lipofectamine TM liposomal transfection reagent were from Invitrogen, USA. The following antibodies were used in this study: EIF3b (cat. no. a301-761a-m), Ki-67 (cat. no. 14-5699-82), MMP-9 (cat. no. MA5-29732) (Invitrogen, USA), β-catenin (cat. no. ab16051), cMyc (cat. no. ab205818), Cyclin D1 (cat. no. ab62151) (Abcam, USA). Matrigel was purchased from Bio-Rad, and Transwell Chamber was purchased from Corning.

Clinical specimens

We collected 45 breast cancer samples, including 31 ductal carcinoma and 14 lobular carcinoma as well as their adjacent normal tissues from patients treated in Shijie Hospital of Dongguan between 2013 and 2021. All patients underwent surgery without anti-tumor therapy, such as radiotherapy, chemotherapy, or endocrine therapy. Our study was approved by the Ethics Committee of Shijie Hospital of Dongguan.

Immunohistochemistry (IHC) staining

The expression of eIF3b in tumors and the paired normal tissues was examined by IHC. The positive eIF3b expression was scored according to the ratio of positive cells: 0 = ratio < 5%, 1 = ratio 5%-24%, 2 = ratio 25%-49%, 3 = ratio 50%-74%, 4 = ratio ≥ 75%, and by the intensity of positive cells: 0 = none, 1 = yellow, 2 = faint yellow, 3 = brown. The product of the two scores < 6 was considered negative expression, while ≥ 6 was positive expression.

Cell culture and transfection

Breast cancer cell lines BT549, MDA-MB-231, T47D, and MCF-7 as well as normal breast cell MCF 10A were obtained from the Chinese Academy of Science's Cell Bank (Shanghai, China). All cells were cultured in RPMI 1640 medium (containing 10% FBS) at 37°C with 5% CO_2.

For eIF3b knockdown experiments, MCF-7 cells and MDA-MB-231 cells were transfected with either a non-specific control siRNA (Scramble group) or with eIF3b-siRNA (SieIF3b group). siRNA was purchased from Shanghai Boshan Biological Co., Ltd., and the sequence was as follow: 5'-GCATCTATGAAACTCCTTCTA-3' and 5'-TTCTCCGAACGTGTCACGT-3'. Transfection was conducted using Lipofectamine TM 2000 (Invitrogen, USA) according to the manufacturer's instructions. Briefly, MCF-7 cells and MDA-MB-231 cells were seeded into 6-well plates and cultured overnight before transfection with a non-specific control siRNA (Scramble group cells), eIF3b-siRNA (20 nM, sieIF3b group), or mock transfection (Control group). The cells were harvested 24 h after transfection.

Real time quantitative PCR (RT-qPCR)

Total RNA was extracted using Trizol RNA extraction kit. Routine RT-PCR were carried out using the following eIF3b-specific primers: 5'-CGGTGCCTTAGCGTTTGTG-3' (upstream) and 5'-CGGTCCTTGTTGTTCTTCTGC-3' (downstream).

Western blot analysis

Cells were lysed in RIPA buffer and cleared by centrifugation to obtain total protein. After quantification by the Bradford method, proteins were separated by SDS-PAGE and transferred

onto PVDF membranes. The membrane was then blocked with 5% skim milk and incubated with the following primary antibodies: EIF3b (1:1000, Invitrogen), Ki-67 (1:1000, Invitrogen), MMP-9 (1:1000, Invitrogen), β-catenin (1: 1000, Abcam), cMyc (1:1000, Abcam), Cyclin D1 (1:1000, Abcam) and β-actin (1:1000, Invitrogen). After extensive washing, the membrane was incubated with the corresponding secondary antibody, and the protein band was developed by ECL. Gray-scale values were measured and analyzed using Quantity One software.

Cell viability and proliferation

CCK-8 assay was used to determine the cell viability. Briefly, cells were seeded at 1×10^4/mL per well, in triplicate, in 24 well plate. CCK-8 solution (APExBIO, Houston, USA) (10 μL/well) was added to each well at different time points: 0 h, 24 h, 48 h, 72 h and 96 h for 4 h, and the absorbance value was measured at 450 nm using a spectrophotometer. To assess cell proliferation, colony formation assay was performed. Briefly, cells were seeded at 1×10^4/mL per well, in triplicate, cultured for 14 days, and fixed with 4% paraformaldehyde. After staining with crystal violet solution, the number of colonies (> 50 cells) was counted and photographed under a microscope.

Transwell assay

For invasion assays, the polycarbonate membranes of transwell chambers were evenly coated with culture medium containing 6.7% matrigel for 1 h at 37°C. Then, 2×10^4 cells/well in serum free medium were seeded on the upper chambers, while regular RPMI 1640 medium containing 10% FBS were added to the lower chamber of transwell. Cells were cultured at 37°C, 5% CO_2, for 36 h before the chambers were removed and the cells on the top side of the membrane were gently swabbed with Q-tip. Cells invaded to the lower side of the membrane were fixed by formaldehydein, stained by crystal violet solution, and examined under microscope (magnification, 100 ×). The number of cells were counted in five random fields, and mean values were calculated. The experiment was repeated three times independently. For migration assays, same procedure as for invasion assay was used except that the membrane on transwell chambers was not coated with Matrigel.

Wound healing assay

Wound healing assay was also used to assess the ability of cell migration. Briefly, MCF-7 cells (2×10^5) and MDA-MB-231 cells (2×10^5) were seeded in 6-well plates and cultured until the cells were in 100% confluent. Then, a 200 ul pipette tip was used to scratch the cell monolayer to create artificial wound. After washing with PBS, the cells were cultured in serum free medium. The wound closure was calculated by comparing the gaps at time 0 and at 24 h of culture.

Lentiviral plasmid construction and transfection

The eIF3b-shRNA-GFP and eIF3b expression sequences were obtained from Boshan Company (Shanghai, China) and were cloned into lentiviral vector. Lentivirus expressing these sequences were produced and used to infect MCF-7 cells and MDA-MB-231 cells. Cells were collected 24-48 h after infection for further analysis.

Animal tumor model

Female BALBc mice (5 weeks old, weight 16-19 g), were purchased from the Laboratory Animal Center of the Army Military Medical University (license number SCXK (Chongqing) 2012-0005) and were divided into three groups (n = 5/group): eIF3b-shRNA-expressing, empty vector-expressing, and mock infection control. MCF-7 cells or MDA-MB-231 cells were used for this experiment. To generate tumors in fat pad, cells (5×10^6/mL in 0.2 mL PBS) were injected into the fourth fat pad on the left side of the abdominal wall. The tumor growth was monitored every 5 days, and the tumor volume was calculated using the formula: tumor volume (V) $(mm)^3 = a \times b^2/2$, where (a) was the maximum longest diameter, while (b) was the maximum vertical transverse diameter. Mice were sacrificed on day 30 post injection, and the tumor mass and lung tissue were dissected and snap-frozen or fixed in PFA for RNA/protein extraction or IHC staining, respectively.

Statistical analysis

SPSS 21.0 was used for statistical analysis. T-test or one-way ANOVA was used to compare the difference between two groups, while the Chi-squared test was used to compare the difference among groups of categorical data.

Table 1. Relative eIF3b mRNA expression levels and eIF3b protein expression positivity rates in breast cancer tissues from patients with different clinical characteristics (n = 45)

Variable	n	eIF3b mRNA ($\bar{x}$ ± s)	eIF3b protein, n (%)
Age (years)			
< 50	20	2.81 ± 1.09	15 (75.00)
≥ 50	25	2.87 ± 1.17	19 (76.00)
Breast cancer types			
Ductal carcinoma	31	2.83 ± 1.34	23 (74.19)
Lobular carcinoma	14	2.89 ± 1.02	11 (78.57)
Tumor diameter (cm)			
≤ 2	12	2.80 ± 1.19	9 (75.00)
> 2	33	2.87 ± 1.27	25 (75.76)
Lymph node metastasis			
Yes	24	3.65 ± 1.46*	22 (91.67)*
No	21	1.95 ± 0.65	12 (57.14)
Histological grade			
1	9	2.78 ± 1.01	7 (77.78)
2	26	2.86 ± 1.39	19 (73.08)
3	10	2.89 ± 1.29	8 (80.00)
TNM			
I-II	18	2.21 ± 0.75*	9 (50.00)*
III-IV	27	3.29 ± 1.72	25 (92.59)

Notes: *$P < 0.05$.

Results

eIF3b expression was upregulated in breast cancer tissues and cell lines

To study the function of eIF3b in the tumorigenesis of breast cancer, we examined its expression in breast cancer tissue and found that both the eIF3b mRNA level and the positive staining of eIF3b protein were obviously higher in 45 breast cancer tissues than in their normal adjacent tissues. Furthermore, the expression level of eIF3b was related to lymph node metastasis and TNM stage of breast cancer patients, as patients with III-IV TNM stage and/or lymph node metastasis showed the highest expression levels (**Table 1**). Consistently, compared with MCF 10A, we found that both eIF3b mRNA and protein levels were markedly increased in the four breast cancer cell lines (MDA-MB-23, BT549, MCF-7 and T47D) we examined (**Figure 1A**, **1B**). Hence, our data suggested that eIF3b might not only participate in breast cancer carcinogenesis, but also promote breast cancer growth, progression, and metastasis.

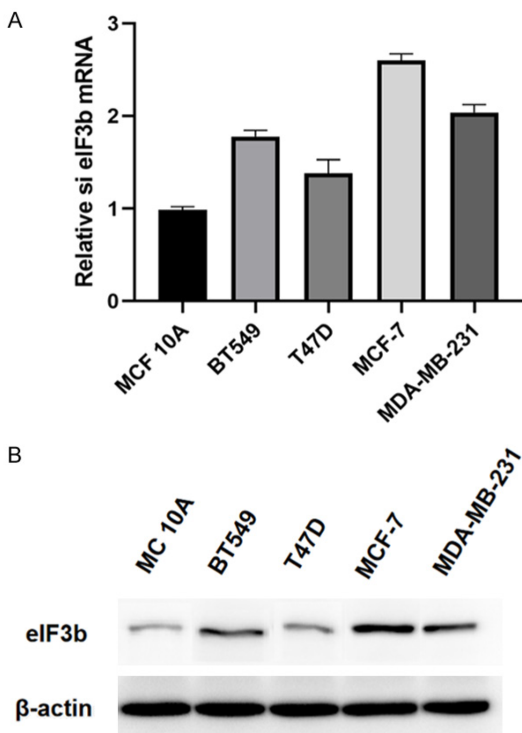


Figure 1. eIF3b expression was up-regulated in breast cancer cell lines. The mRNA (A) and protein (B) expression levels of eIF3b in different breast cancer cell lines by WB and RT-PCR.

Knockdown of eIF3b significantly inhibited the malignant progression of breast cancer cells

Due to the relatively higher expression level of eIF3b in MCF-7 cells and MDA-MB-231 cells, we used these two cell lines to study the effect of eIF3b knockdown on cell growth. RT-PCR and western blotting confirmed the successful knockdown of eIF3b by eIF3b-siRNA in MCF-7 and MDA-MB-231 cells (**Figure 2A**, **2B**). CCK-8 assays showed that eIF3b knockdown significantly decreased the cell viability of MCF-7 and MDA-MB-231 (**Figure 3A**). In addition, we performed colony formation assays to evaluate the long-term effect of eIF3b knockdown on cell proliferation and found that eIF3b knockdown inhibited the proliferation of MCF-7 and MDA-MB-231 cells (**Figure 3B**, **3C**). Furthermore, we revealed that eIF3b knockdown significantly suppressed the migratory capacity of MCF-7

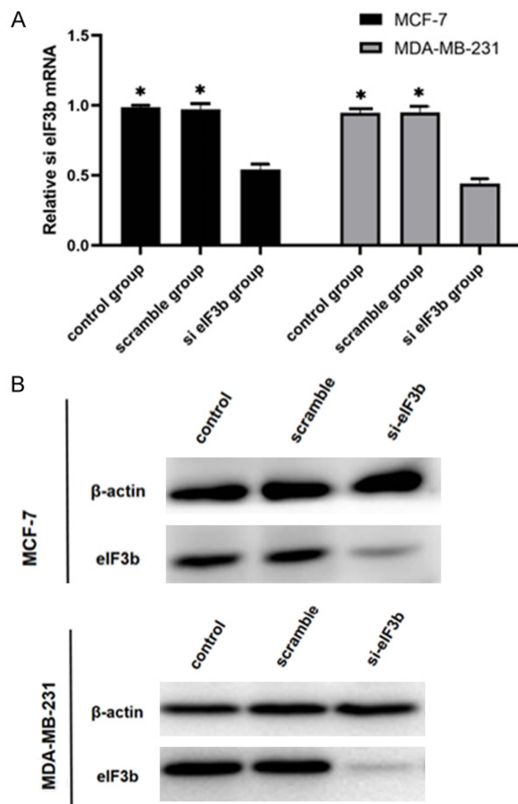


Figure 2. EIF3b gene was effectively knockdown. EIF3b mRNA (A) and protein (B) expression levels were obviously reduced in breast cancer cell lines MCF-7 and MDA-MB-231 treated with eIF3b-siRNA. Notes: vs. si eIF3b group; *$P < 0.05$.

and MDA-MB-231 cells, as determined by both wound healing assay (**Figure 4A**, **4B**) and transwell assay (**Figure 4C**, **4D**). Conversely, eIF3B overexpression significantly enhanced the migration and invasion of MCF-7 and MDA-MB-231 cells (**Figure 4E-H**).

eIF3b knockdown inhibited the growth of xenograft tumor in nude mice

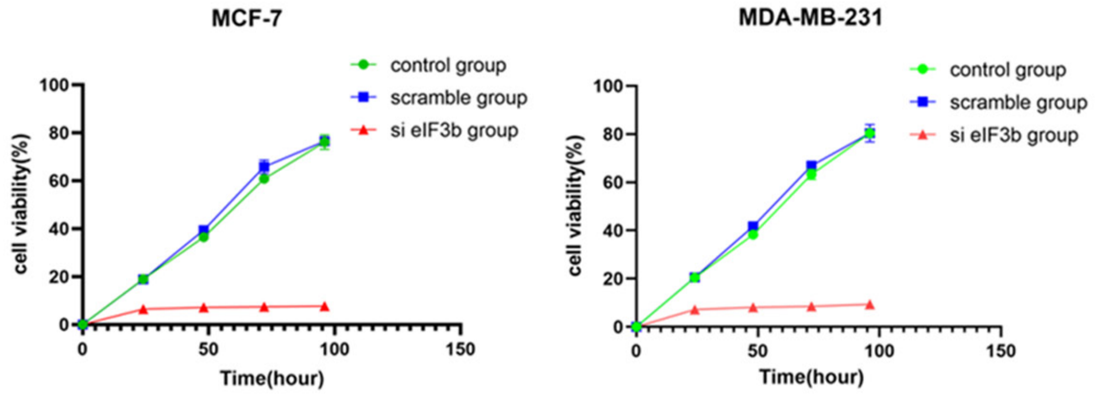
To further investigate the effect of eIF3b knockdown on tumor growth and metastasis in vivo, we first infected MCF-7 and MDA-MB-231 cells with eIF3b-shRNA lentivirus, vector control lentivirus, or mock infection. The high infection efficiency (> 80%) was confirmed by fluorescence microscope at 72 h after infection (**Figure 5A**). Then, these cells were used to establish xenograft tumors in nude mice. We observed that 100% of mice in all three groups developed tumors at day 10 post inoculation, and the mice were sacrificed at day 30 (**Figure 5B**). When comparing the tumor volume, we found that tumors derived from eIF3b-shRNA infected MCF-7 and MDA-MB-231 cells were significantly smaller than those from control- and empty vector-infected cells ($P < 0.05$), while there was no difference in volume between tumors from control- and empty vector-infected cells ($P > 0.05$) (**Figure 5C**). Moreover, we evaluated the role of eIF3b on lung metastasis in the mice of these three experimental groups and found that lung metastasis was also clearly suppressed by eIF3b knockdown, as the number of lung metastatic nodules was markedly decreased (**Figure 6A-C**).

Importantly, we examined the effect of eIF3b silencing on the expression of the proliferation and migration-related markers such as Ki-67 (cell proliferation marker) and MMP-9 (cell migration marker) in the xenograft tumor tissues and found a dramatically reduced expression of them in eIF3b silencing cell-derived tumors ($P < 0.05$; **Figure 7A**, **7B**), whereas there was no difference in the expression of these proteins between samples from the empty vector infection and control groups ($P > 0.05$).

To further explore the functional mechanisms by which eIF3b promoted breast cancer progression, we examined the expression of signaling molecules downstream of the Wnt/β-Catenin pathway in eIF3b knockdown tumors. Significantly, the expression of β-Catenin, cMyc and Cyclin D1 was dramatically lower in the eIF3b-shRNA expressing tumors than in empty vector-expressing tumors and control group ($P < 0.05$; **Figure 7C**, **7D**). As expected, their expression was similar between the empty vector infected and control group ($P > 0.05$), suggesting that eIF3b might activate Wnt/β-Catenin pathway, resulting in an accelerated tumor progression.

Discussion

Accumulating evidence has indicated that eIF3b participates in the signaling pathways that are involved in regulating cell differentiation, apoptosis, and invasion/migration through its role in controlling protein translation [4-7]. For example, Wang et al. found that eIF3b gene silencing effectively reduced colon cancer cell proliferation [8]. Similarly, silencing eIF3b gene


A
MCF-7
control group
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cell viability(%)
Time(hour)
MDA-MB-231
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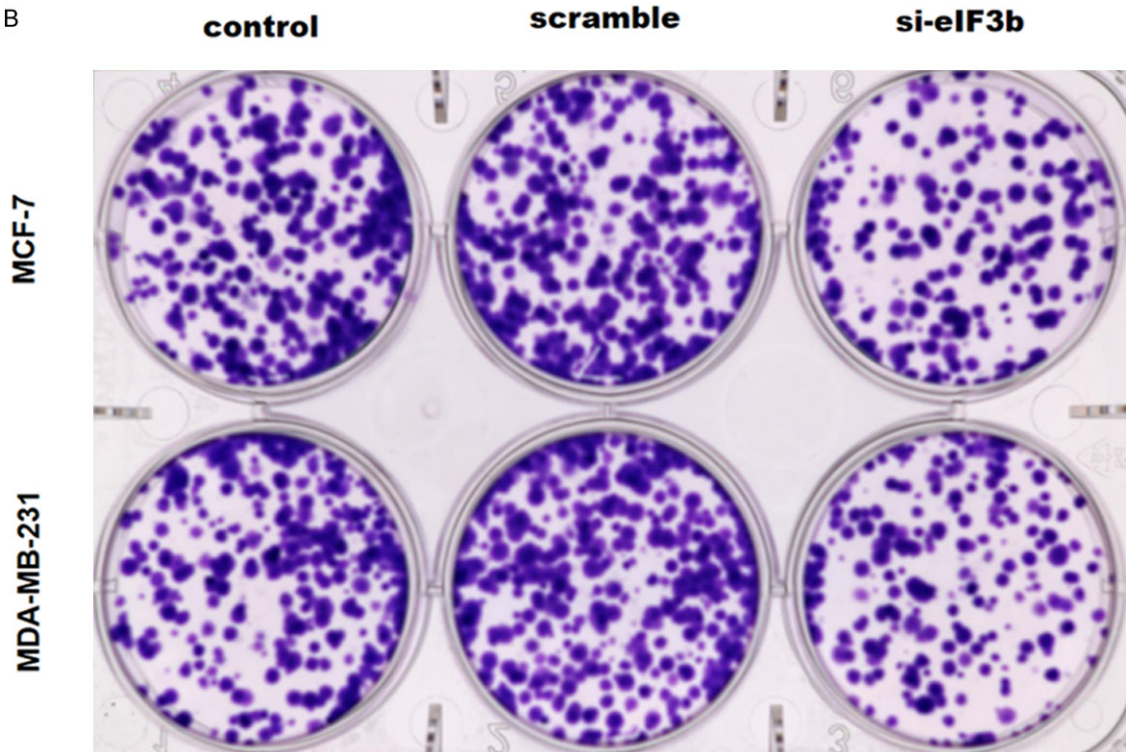
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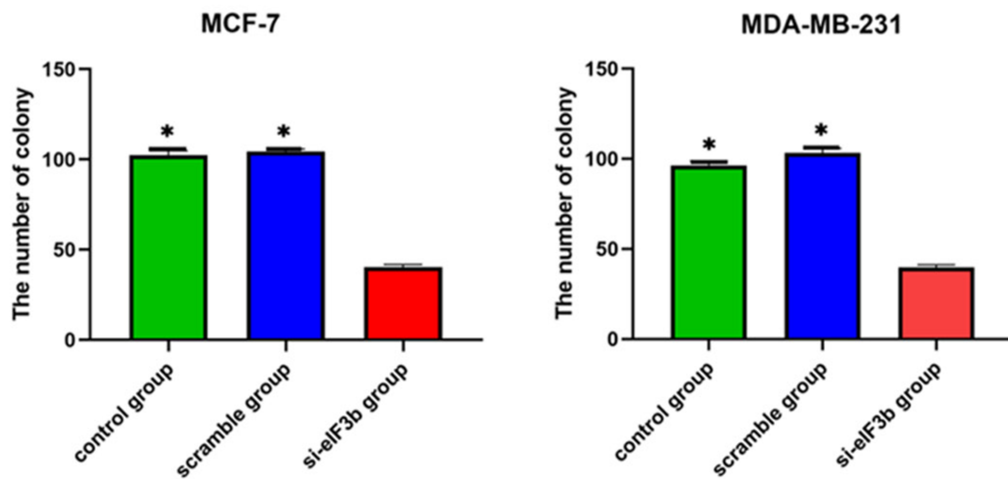
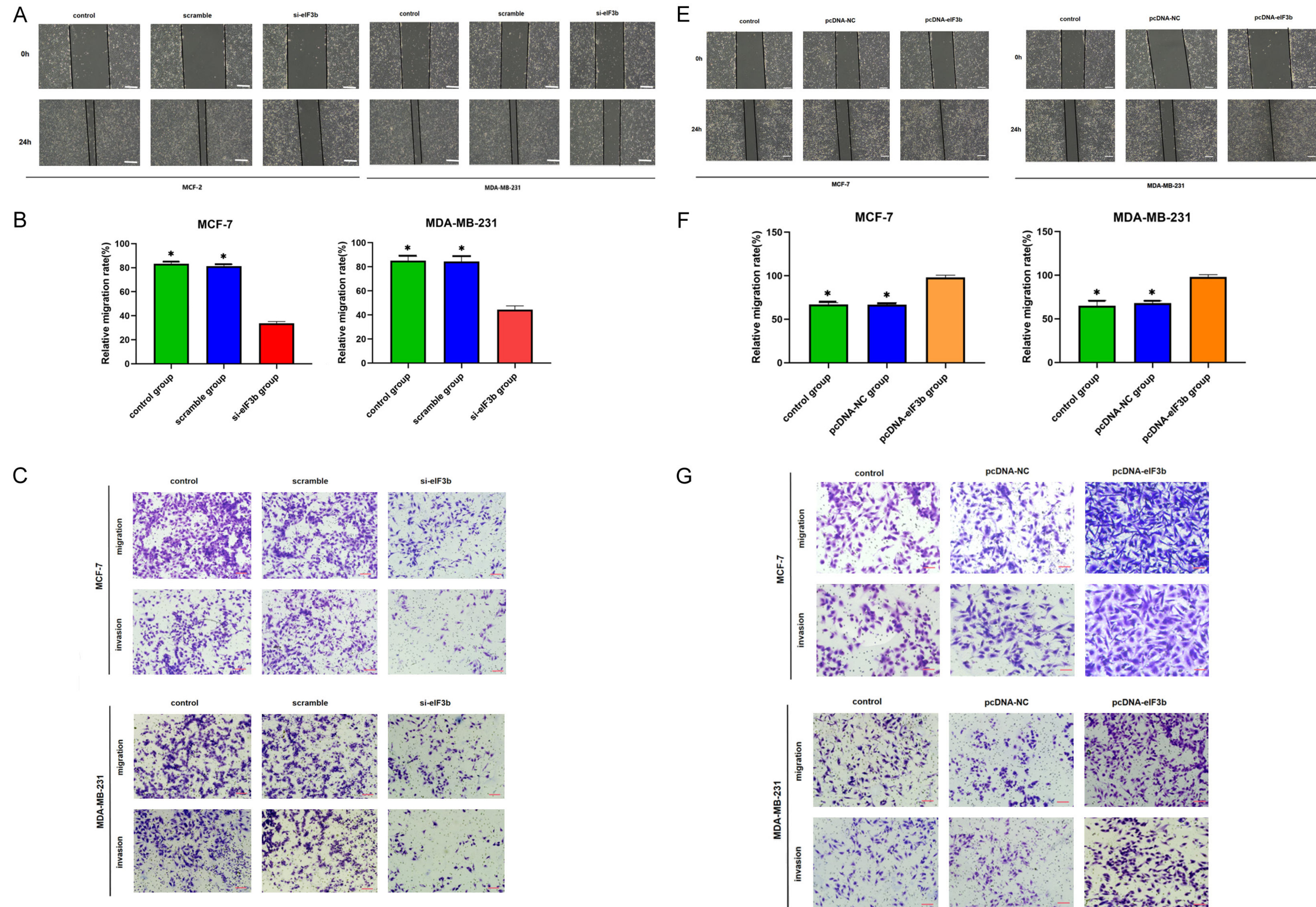

C
MCF-7
The number of colony
control group
scramble group
si-eIF3b group
MDA-MB-231
The number of colony
control group
scramble group
si-eIF3b group

Figure 3. EIF3b knockdown suppressed cell proliferation in breast cancer cell lines. A. Breast cancer cell lines MCF-7 and MDA-MB-231 were collected for cell viability measurements using CCK-8 analysis. B. Colony formation assay for MCF-7 and MDA-MB-231 cells following si-eIF3b for 24 h. Scar bar = 50 μm. C. EIF3b knockdown inhibited the proliferation of MCF-7 and MDA-MB-231 cells. **P* < 0.05.



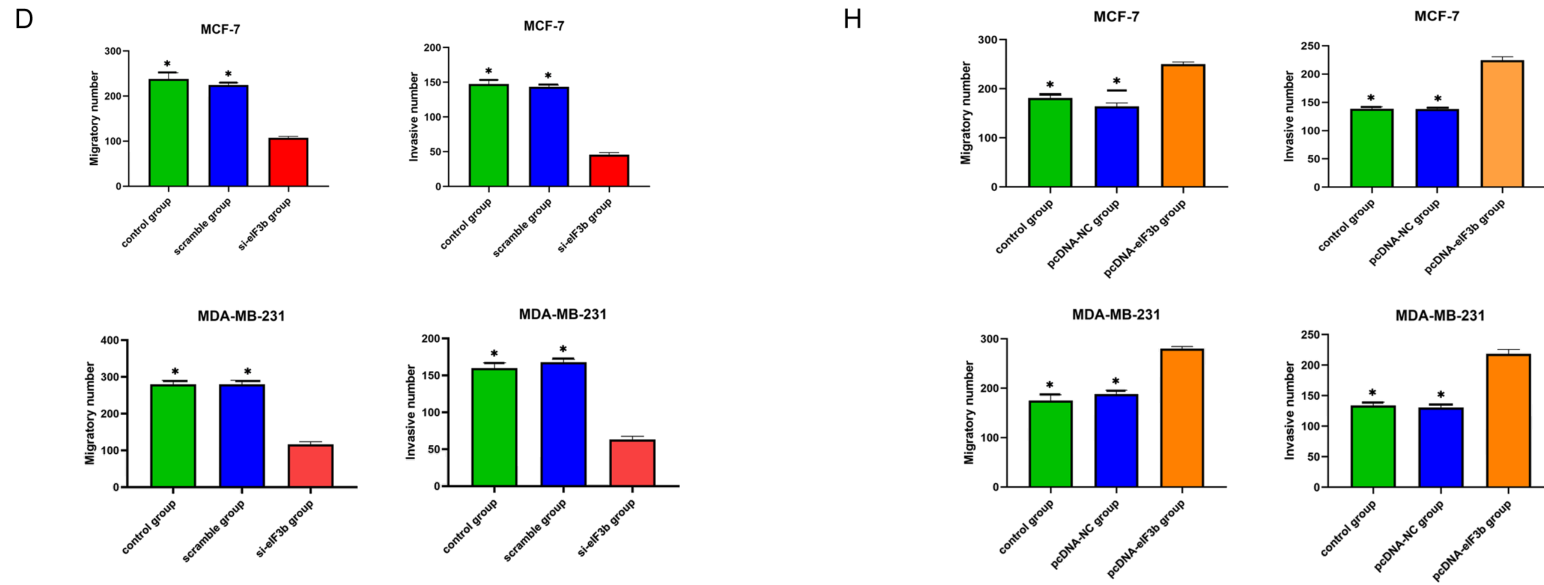


Figure 4. EIF3B knockdown/over expression inhibited/enhanced cell migration and invasion in breast cancer cell lines. MCF-7 and MDA-MB-231 cells were subsequently incubated with si-eIF3b and pcDNA-eIF3b for 24 h, and were then collected for studies as follows: The effect of eIF3b knockdown on migration and invasion of MCF-7 and MDA-MB-231 cells was assessed by wound healing assay (A, B) and transwell analysis (C, D), respectively. The effect of eIF3b overexpression on migration and invasion of MCF-7 and MDA-MB-231 cells was assessed by wound healing assay (E, F) and transwell analysis (G, H), respectively. Scar bar = 200 μm; *$P < 0.05$.

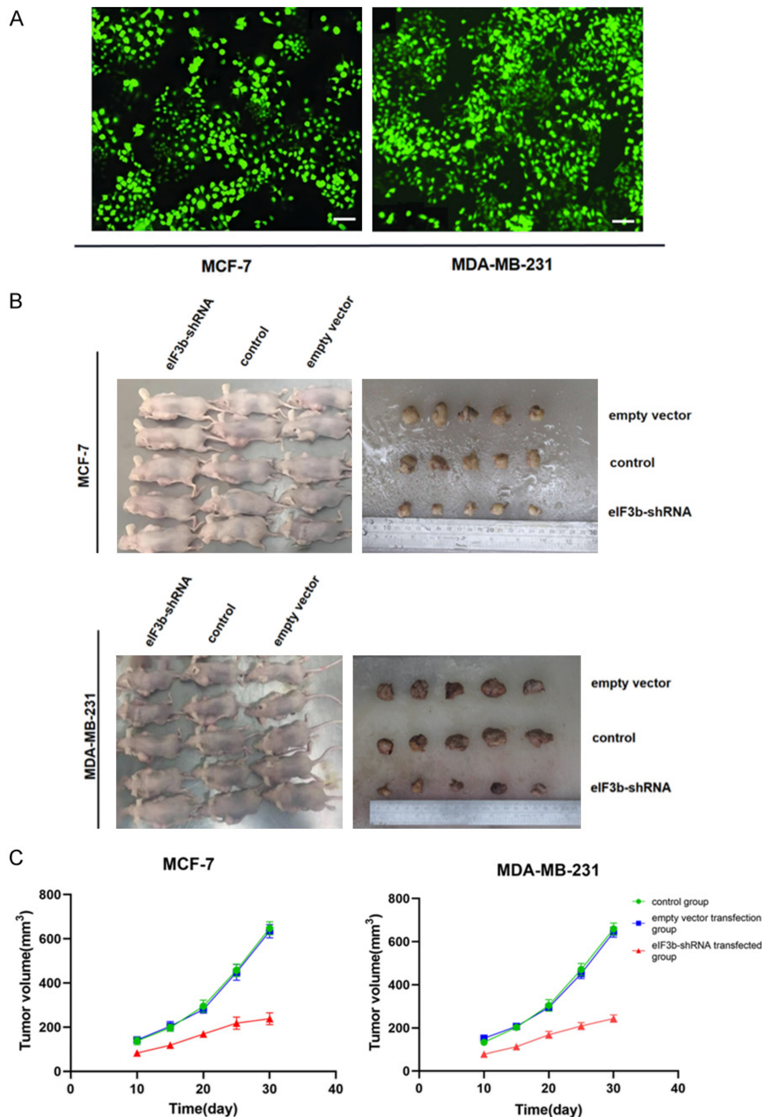


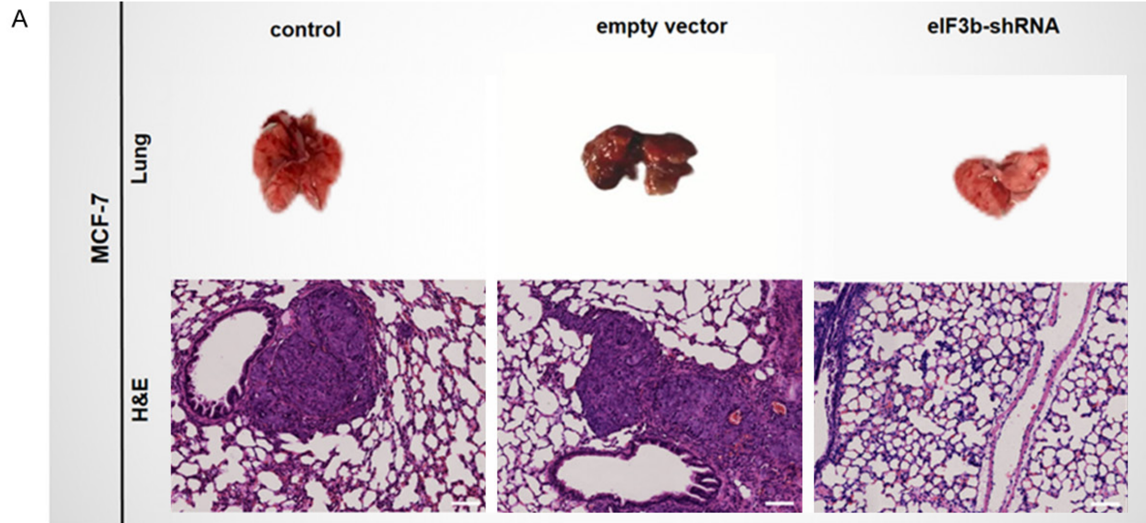
Figure 5. eIF3b knockdown suppresses tumor growth in breast cancer models in vivo. (A) Detection of green fluorescent protein expression in MCF-7 and MDA-MB-231 cells 72 h after lentiviral infection (Scar bar = 100 μm). (B) Nude mice at 30 days after xenotransplant injection; Tumor formation and tumor tissue in nude mice, and comparison of tumor volumes (C).

expression in bladder cancer cells significantly inhibited the development of bladder cancer [9], and Xu et al. reported that downregulation of eIF3b expression inhibited osteosarcoma cells growth [10]. Furthermore, Zang et al. investigated the effect of eIF3b in renal cell carcinoma and concluded that eIF3b contributes to tumor development and may serve as a diagnostic marker of renal cancer as well as a therapeutic target for the treatment of renal cancer [11]. Consistently, in 2021, Zhu et al. found that the upregulation of eIF3b was associated with the poor prognosis of pancreatic cancer and that eIF3b was involved in the regulation of tumor cell proliferation, migration, and invasion [12]. Other studies also reported the similar results. Tian Y et al. reported in 2018 that the expression of eIF3b was elevated in non-small cell lung cancer, and the expression level was related to tumor stage and grade, while the downregulation of eIF3b expression inhibited the proliferation and invasion of lung cancer cells and prostate cancer cells in vitro [13]. Moreover, Fang et al. indicated that eIF3b promoted the proliferation and mobility of gastric cancer cells via regulating tumor-promoting molecules [6]. Hence, eIF3b is important for the development and progression of multiple tumors; however, the effects of eIF3b and the relevant signaling pathways on regulating the growth, apoptosis, and migration/invasion of breast cancer have not been reported previously.

In this study, we revealed that eIF3b was expressed at higher level in human breast cancer cell lines and tumor samples. In addition, both eIF3b mRNA and protein levels in breast cancer tissues were closely associated with lymph node metastasis and TNM stage. Consistently, silencing eIF3b by siRNA suppressed the viability and proliferation of breast cancer cells in vitro, as determined by CCK-8 assay and colony formation assay.

Tumor infiltration and metastasis are not only related to primary tumor cell proliferation and growth, but also requires the ability of tumor cells to break through surrounding tissue and vascular basement membrane. Thus, the strong migration and invasion abilities of tumor cells, as well as the survival ability, are associ-

A



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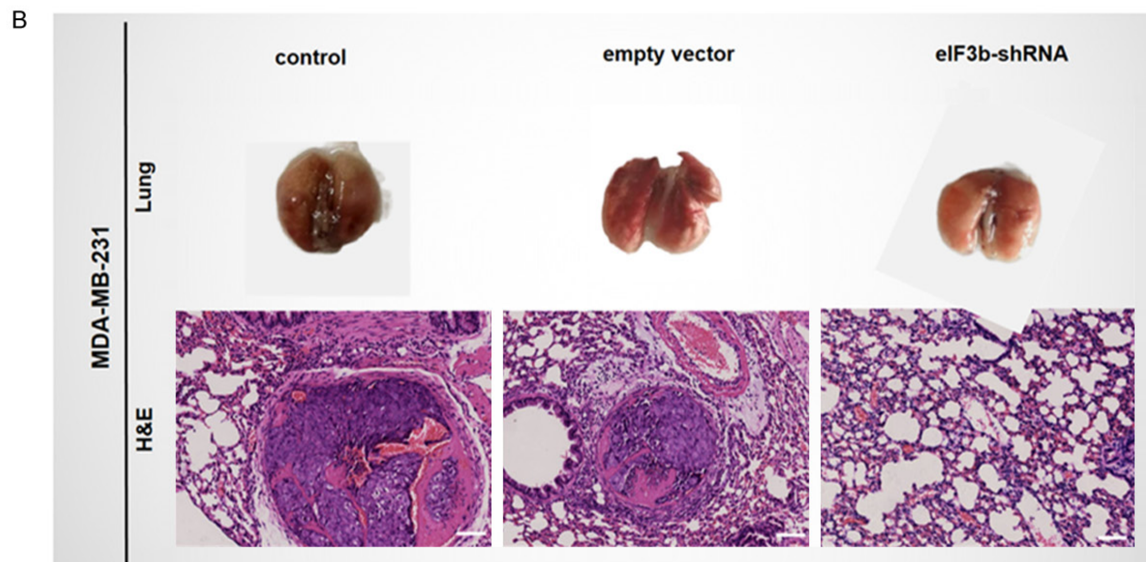

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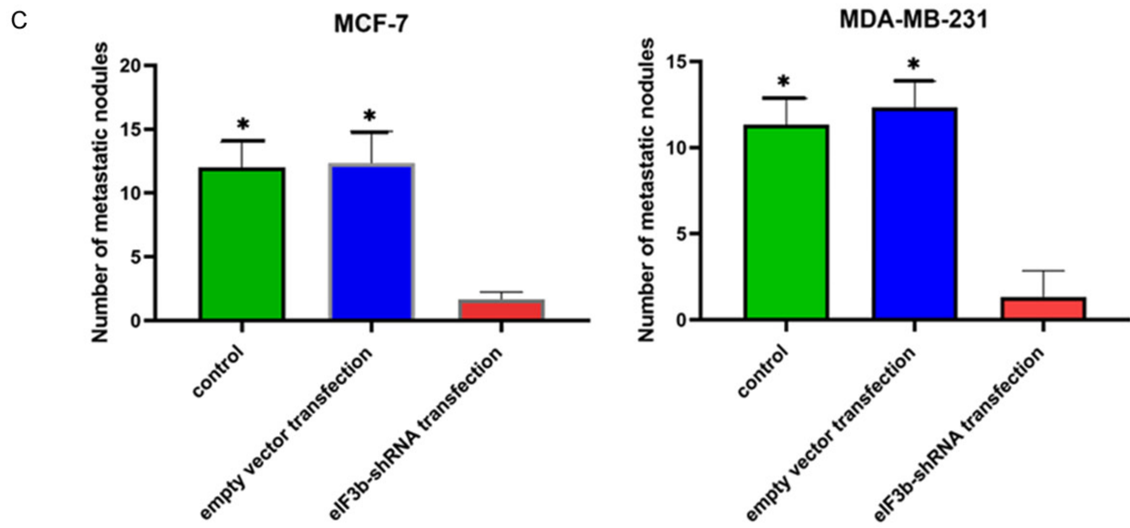

Figure 6. EIF3b-knockdown suppresses tumor metastasis in breast cancer models in vivo. A, B. Whole lung tissues, HE staining in lung sections from the three groups of nude mice were exhibited. Scar bar = 100 μm. C. Number of metastatic nodules on the lung were shown. Values represent the mean ± SEM (n = 5 per group). *P < 0.05 versus eIF3b-shRNA group.

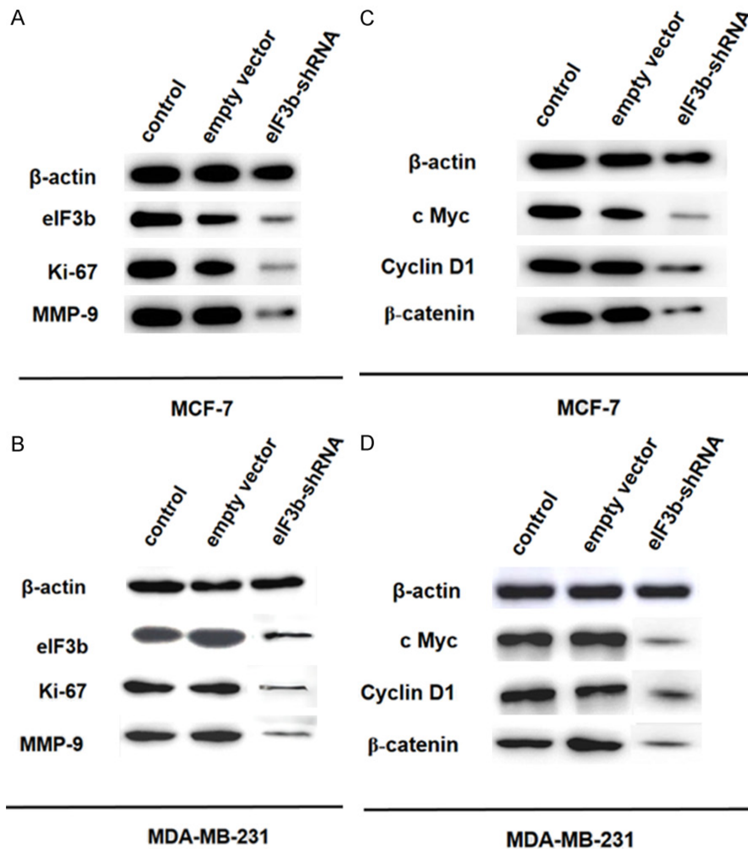

Figure 7. The mechanisms of eIF3b on the proliferation, migration and invasion of breast cancer cell lines MCF-7 and MDA-MB-231 in vivo. A, B. EIF3b, Ki-67 and MMP-9 protein in three groups were examined by western blotting, the expression of eIF3b, Ki-67 and MMP-9 was dramatically lower in the eIF3b-shRNA expressing tumors than in empty vector-expressing tumors and control group. C, D. β-catenin, c Myc and Cyclin D1 protein in three groups was determined by western blotting, the expression of β-catenin, cMyc and Cyclin D1 was dramatically lower in the eIF3b-shRNA expressing tumors than in empty vector-expressing tumors and control group.

ated with the increased malignant progression and tumor recurrence as well as metastasis. Therefore, determining how to effectively prevent and inhibit breast cancer migration and invasion is vital for the prognosis of breast cancer. In this study, we explored the effect of eIF3b on migration and invasion by using wound healing assay and transwell assay, and our results demonstrated that eIF3b knockdown inhibited the mobility of breast cancer cells. Conversely, eIF3b overexpression showed the opposite effects.

More importantly, to determine the physiological effect of eIF3b on tumor growth in vivo, we established mouse xenograft tumor model by injecting eIF3b knockdown-MCF-7 and -MDA-MB-231 cells into nude mice [14-16]. We observed that tumors derived from eIF3b-silencing cells were significantly smaller than those derived from control and empty vector-expressing cells. Furthermore, the lung metastasis in eIF3b-silencing cells-injected nude mice was markedly inhibited. Together, these findings suggested that eIF3b inhibition could significantly suppress tumor growth and pulmonary metastases in vivo.

The cell proliferation nuclear antigen, Ki-67 protein, is commonly used in clinical practice as a marker of malignant tumors, which reflects malignant cell proliferation in tumor tissues. On the other hand, MMP-9 is a marker for the migration capability of malignant tumor cells, as the expression level of MMP9 is closely related to the invasive ability of malignant tumor and patient prognosis. Here, we found that the expression of Ki-67 and MMP-9 was significantly lower in the xenograft tumors derived from eIF3b-silencing cells, indicating that eIF3b knockdown can inhibit Ki-67 and MMP-9 expression in nude mice. Collectively, our data suggest that eIF3b inhibition attenuates breast cancer cell proliferation, tumor growth, and metastasis; thus, eIF3b may serve as a potential therapeutic target for breast cancer treatment.

Wnt/β-Catenin signaling is an important regulatory pathway in eukaryotes, which determines

cell differentiation fate during development. In addition, activated Wnt signaling can enhance the accumulation of β-catenin in the nucleus, where it transactivates proto-oncogenes such as cMyc, leading to tumorigenesis [17-19]. Several studies [6, 11, 17, 18, 20, 21] have demonstrated that knockdown of eIF3b could inhibit the proliferation, migration, and invasion of tumor cells; however, downregulating Wnt signaling pathway induces apoptosis in acute myeloid leukemia and endometrial cancer cells, suggesting that eIF3b could affect tumorigenesis through Wnt/β-Catenin signaling pathway. Furthermore, Xu et al. [10] have also reported that eIF3b can promote tumor development through the activation of the Wnt/β-Catenin pathway. In this study, we were the first to report that eIF3b downregulation suppressed the proliferation and migration of breast cancer cells, whereas eIF3b knockdown exhibited the opposite effects. More importantly, our data suggested that the effect of eIF3b on the malignant phenotype was through blocking the Wnt/β-catenin pathway in breast cancer. Specifically, we found that the expression of Wnt/β-catenin signaling downstream proteins, β-catenin, cMyc and Cyclin D1, was inhibited in tumors derived from eIF3b-silencing cells. Since the growth and pulmonary metastases of these tumors were also obviously suppressed, we proposed that knockdown of eIF3b could inhibit tumor progression through Wnt/β-catenin pathway, which may be closely associated with the blockade of cell cycle.

In conclusion, our study revealed an abnormal upregulation of eIF3b in human breast cancer, which was associated with poor prognosis. Downregulation of eIF3b effectively suppressed the malignant phenotype of breast cancer in vitro and in vivo. Furthermore, the influence of eIF3b on the proliferation, migration, and invasion of breast cancer cells might be related to the Wnt/β-catenin pathway. Collectively, our data provide the evidence of applying eIF3b as a potential therapeutic target for the treatment of patients with breast cancer. Thus, the more detailed molecular mechanism underlying the function of eIF3b in breast cancer should be further explored.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yanhui Li, Department of Pathology, Shijie Hospital, No. 35 Chonghuan West Road, Shijie Town, Dongguan, Guangdong, China. Tel: +86-13751464606; E-mail: 23175756@qq.com

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