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Downregulation of MUC1 Inhibits Proliferation and Promotes Apoptosis by Inactivating NF-κB Signaling Pathway in Human Nasopharyngeal Carcinoma*

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Abstract **Objective** To investigate the effect of mucin 1 (MUC1) on the proliferation and apoptosis of nasopharyngeal carcinoma (NPC) and its regulatory mechanism. **Methods** The 60 NPC and paired para-cancer normal tissues were collected from October 2020 to July 2021 in Quanzhou First Hospital. The expression of MUC1 was measured by real-time quantitative PCR (qPCR) in the patients with PNC. The 5-8F and HNE1 cells were transfected with siRNA control (si-control) or siRNA targeting *MUC1* (si-MUC1). Cell proliferation was analyzed by cell counting kit-8 and colony formation assay, and apoptosis was analyzed by flow cytometry analysis in the 5-8F and HNE1 cells. The qPCR and ELISA were executed to analyze the levels of TNF-α and IL-6. Western blot was performed to measure the expression of MUC1, NF-κB and apoptosis-related proteins (Bax and Bcl-2). **Results** The expression of MUC1 was up-regulated in the NPC tissues, and NPC patients with the high MUC1 expression were inclined to EBV infection, growth and metastasis of NPC. Loss of MUC1 restrained malignant features, including the proliferation and apoptosis, downregulated the expression of p-IκB、p-P65 and Bcl-2 and upregulated the expression of Bax in the NPC cells. **Conclusion** Downregulation of MUC1 restrained biological characteristics of malignancy, including cell proliferation and apoptosis, by inactivating NF-κB signaling pathway in NPC.

Key words mucin 1, nasopharyngeal carcinoma, NF-κB signaling pathway, proliferation, apoptosis
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Nasopharyngeal carcinoma (NPC) is an epithelial carcinoma occurring in the crypt of the nasopharynx. It had shown that non-keratinized NPC accounted for about 95%[1], which was closely related to Epstein-Barr virus (EBV) infection[2]. In addition, progress of NPC was accelerated by inflammation[3]. According to the international center for research on cancer, incidence of NPC was nearly 133 000 per year, accounting for 0.7% of new cancer diagnosed and the mortality was about 80 000 per year, accounting for 0.8% of cancer deaths[4]. The distribution of NPC was highly uneven[5], and 70% of new diagnosed cases was occurred in East and Southeast Asia, especially in China, where 3 out of

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100 000 people had suffered from NPC[6]. With the change of living customs and population migration, the incidence of NPC had decreased by 1%−5% every year in worldwide[7], and the 5-year survival rate of NPC was 63.3%−71.4%[8].

The occurrence and development of NPC were a complex process involving multiple genes or signaling pathways. NF-κB activation was one of the causes for promoting NPC progression. circBART2.2 encoded by EBV up-regulated the expression of PD-L1 through activating IRF3 and NF-κB, resulting in NPC immune escape[9]. It was demonstrated that silencing of NKILA increased the invasive motility of NPC cells by NF-κB pathway[10]. E2F was highly expressed and played a promoting role in inflammation and tumorigenesis of NPC[11].

Mucin 1 (MUC1) encodes a membrane bound protein and plays a crucial role in forming protective mucus barrier on surface of the epithelium[12]. Increased evidences had suggested that the abnormal expression of MUC1 was closely related to tumors, such as colorectal cancer[13], breast cancer[14] and gastric cancer[15]. It was reported that MUC1 was associated with NPC[16], however, the underlying mechanism by which MUC1 regulates development of NPC remains unclear.

MUC1 promoted the immune escape of triple-negative breast cancer cells through increasing the expression of PD-L1 by activating the NF-κB signaling pathway[17]. It was showed that MUC1 accelerated the proliferation and invasion of lung carcinoma cells by NF-κB signaling pathway[18]. MUC1 was highly expressed in prostate cancer and the proliferation was promoted through the NF-κB-MUC1 loop pathway[19]. It was verified that MUC1 downregulated expression of LINE-1 and CDH1 through methylating DNA promoter induced by NF-κB, resulting to the development of breast cancer[20]. In brief, the NF-κB signaling pathway was activated by MUC1 in a variety of cancers.

Based on the abnormal expression of MUC1 in NPC patients and the ability of MUC1 to activate the NF-κB pathway in other cancers, we want to prove that MCU1 regulates malignant features of NPC cells by NF-κB pathway in the present study.

1 Materials and methods

1.1 Samples collection and ethical approval

The 60 patients diagnosed NPC were enrolled at the otolaryngological department of Quanzhou First Hospital from October 2020 to July 2021. Sixty tumour and sixty paired paracancer normal tissues were collected. All patients signed informed consent at the time of surgery. This study was approved by the Ethics Committee of Quanzhou First Hospital (approval No. (2019)011), and abided by principles in the Declaration of Helsinki. All patients signed informed consent prior to samples collection.

1.2 Cell culture

The normal human nasopharyngeal epithelial cells (NP69) and NPC cells (CNE1, 5-8F and HNE1) were obtained from ATCC. The cells were cultured in DMEM (for NP69 and HNE1, Gibco, USA) or RPMI 1640 (for CNE1 and 5-8F, Gibco, USA). All medium was supplement with 10% fetal bovine serum (FBS, Gibco, USA) and 1% penicillin-streptomycin solution (PB180120, Pricella, China). The NPC cells were cultured at 37℃ in a 5% CO_2 saturated humidity incubator.

1.3 Cell transfection

The expression of MUC1 was interfered by small interfering RNA (si-RNA). The siRNA control (si-control, 5'-UUCUCCGAACGUGUCACGUTT-3') and MUC1 si-RNA (si-MUC1, 5'-GUUCAGUGCCC-AGCUCUAC-3') were designed and synthesized by GenePharma (Shuzhou, China). The 5-8F and HNE1 cells were transfected with siRNAs (si-control, si-MUC1) by Lipofectamine 3000 in according to the manufacturer's instruction when it was grown to 70% confluence.

1.4 Real−time quantitative PCR （qPCR） analysis

The expression of MUC1, TNF-α and IL-6 were analyzed by qPCR analysis. Briefly, RNAs from tissues and cells were extracted by Trizol reagent (R0016, Beyotime, China) in according to the manufacturer's instruction. RNAs concentration was detected by a spectrophotometer (NanoDrop 2000, Thermo, USA). The All-One RT Mastermix Kit (G492, abm, Canada) was used to generate cDNA in

according to the manufacturer's instruction. Finally, the expression of genes were determined on a thermal cycler (CFX Connect Real-Time System, Bio-Rad, USA) by EvaGreen qPCR MasterMix (MasterMix-S, abm, Canada) in according to manufacturer's instruction, following parameters: pre-denaturation for 10 min at 95℃; at 95℃ 15 s, 60℃ for 40 cycles. The β-actin was used as internal control. The $2^{-\Delta Ct}$ method was used to calculate the expression of genes. The primers were listed in Table 1.

Table 1 The primers sequences of qPCR in this study

Name	Sequence of bases （5'-3'）
MUC1 forward	TCAGCTTCTACTCTGGTGCACAA
MUC1 reverse	ATTGAGAATGGAGTGCTCTTGCT
TNF-α forward	CATCTTCTCAAAATTCGAGTGACAA
TNF-α reverse	CCCAACATGGAACAGATGAGGGT
IL-6 forward	AGGATACCACTCCCAACAGACCT
IL-6 reverse	CAAGTGCATCATCGTTGTTACTAC
β-Actin forward	TGGCACCCAGCACAATGAA
β-Actin reverse	CTAAGTCATAGTCCGCCTAGAAGCA

1.5 Antibodies

All antibodies were purchased from Beyotime (China). The antibodies were listed as follow: MUC1 rabbit monoclonal antibody (AG2685, 1∶1 000), IκB rabbit monoclonal antibody (AF1282, 1∶ 1 000), phospho-IκB (Ser32) rabbit monoclonal antibody (AF1870, 1∶1 000), NF-κB rabbit monoclonal antibody (AF1234, 1∶ 1 000), phospho-NF-κB (Ser536) rabbit polyclonal antibody (AF5881, 1∶500), Bax rabbit polyclonal antibody (AF0057, 1∶ 500), Bcl-2 rabbit polyclonal antibody (AF0060, 1∶ 500), β-actin rabbit monoclonal antibody (AF5003, 1∶2 000) and HRP-labeled goat anti-rabbit IgG (A0208, 1∶2 000).

1.6 Western blot

The samples and cells transfected with or without si-MUC1 were collected and lysed in pre-cooled RIPA (P0013B, Beyotime, China) on ice for 1 h. The lysates of samples and cells were centrifuged at 13 300*g* for 30 min in a 4℃ centrifuge. The supernatant of lysates was collected. The protein concentration was determined using a spectrophotometer (NanoDrop ND-2000, Thermo, USA). The proteins were separated by 12% SDS-PAGE, transferred into the PVDF membrane (IPVH00010, Millipore, Germany). Non-specific proteins were blocked with 5% skim milk for 2 h at room temperature (RT). Then, the membrane was incubated with specific antibodies for 2 h at RT, subsequently incubated with secondary antibodies for 1 h at RT. The protein bands were visualized using BeyoECL Star (P0018AS, Beyotime, China) by gel imaging system (Chemidoc MP, Bio-Rad, USA). Finally, the ImageJ software (V1.8.0.112) was used to analyze the expression of proteins.

1.7 Cell counting kit−8 （CCK−8） analysis

The proliferation of cells was analyzed by CCK-8 analysis. The 5-8F and HNE1 cells were planted into 96-well at cell concentration of 1 000/well, transfected with si-control or si-MUC1 and continually cultivated for the indicated times. About 10 μl CCK-8 (C0038, Beyotime, China) solution/well was added in the cells and cells were cultivated in a 37℃ incubator for 1 h in according to the manufacturer's protocol. Finally, the absorbance (*A*) was measured using a spectrophotometer at the wavelength of 450 nm.

1.8 Colony formation assay

The 5-8F and HNE1 with si-control or si-MUC1 were resuspended in complete medium. The cells were planted into 24-well plate at 1 000 per well, and cultured for 10 d at 37℃ in a 5% CO_2 saturated humidity incubator. The cells were fixed with 4% paraformaldehyde (P0099, Beyotime, China) at RT for 30 min and stained with crystal violet (C0121, Beyotime, China) at RT for 5 min. The images of colonies were photographed using microscope. The number of colonies was calculated using ImageJ software.

1.9 Flow cytometry analysis

The flow cytometry analysis was performed to analyze apoptosis of cells. The 5-8F and HNE1 cells were transfected with si-control or si-MUC1 for 24 h, collected to stain with Annexin V-FITC (C1062M, Beyotime, China) according to the manufacturer's protocol using flow cytometry (BD, USA). Apoptosis was analyzed using FlowJo (v10.5, BD, Switzerland).

1.10 Enzyme−linked immunosorbent assay （ELISA）

The 5-8F cells were transfected with si-control or si-MUC1. The culture supernatant of cells was collected and analyzed using TNF-α (PT518, Beyotime, China) and PGE2 (HB833-Hu, Hengyuan, China) ELISA kits according to the manufacturer's.

protocol Finally, the *A* value was detected using a spectrophotometer.

1.11 Statistical analysis

All data from three independent experiments was presented as the *mean*±standard deviation (*SD*) and analyzed with GraphPad (Prism 8.3) and SPSS 23.0 (IBM). The independent student's *t*-test was executed to analyze the expression of MUC1 in the patients with NPC. The Mann-Whitney U test was executed to analyze the correlation between MUC1 and pathological characteristics of patients with NPC. The Tukey's multiple comparisons of two-way ANOVA were executed to analyze the proliferation, apoptosis and expression of MUC1, TNF-α, IL-6 and NF-κB signaling pathway associated proteins of cells transfected with si-control or si-MUC1. It was considered as statistically significant when $P<0.05$.

2 Results

2.1 The expression of MUC1 was upregulated in patients with NPC

To explore the expression of MUC1 in the patients with NPC, qPCR and Western blot were performed. As shown in Figure 1a, the expression of MUC1 was upregulated in the tumour tissues compared with that in the normal tissues. The samples of three patients were randomly selected to investigate the expression of MUC1 protein by Western blot. Undoubtedly, the results of Western blot were consistent with those of qPCR, which MUC1 protein was increased in the tumour tissues (Figure 1b, c). These results were suggested that MUC1 was highly expressed in NPC.

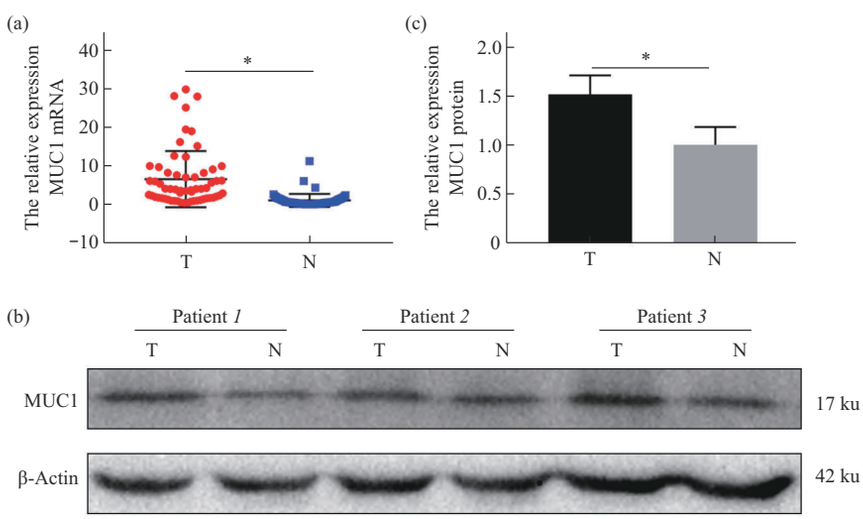

Fig. 1 The expression of MUC1 was up−regulated in the patients with NPC

The samples of 60 tumor and normal tissues were collected. The expression of MUC1 mRNA (a) and protein (b, c) were respectively detected by qPCR and Western blot, which showed that MUC1 was higher expressed in the patients with NPC. T and N respectively mean tumor and normal tissues. Data presented *mean*±*SD*. **P*<0.05, independent *t*-test.

2.2 MUC1 was closely associated with the pathological characteristics of NPC patients

The 60 patients with NPC were divided into low expression and high expression according to the expression of MUC1. The MUC1 expression of patients was arranged in ascending order. The patients were defined as MUC1 low expression group when the MUC1 expression was lower than the median of MUC1 expression; otherwise, the NPC patients were defined as MUC1 high expression. The correlation analysis between the MUC1 expression and the pathological characteristics was performed to explore the role of MUC1 on development of NPC. As shown in Table 2, the gender and age of NPC patients were independent of the expression of MUC1. However, the expression of MUC1 was closely associated with EBV-VCA IgA, size of NPC and metastasis, which indicated that high expression of MUC1 was inclined to EBV infection, growth and metastasis of NPC.

Table 2 Relationship between MUC1 expression and clinicopathological variables

Variables	Total	MUC1 expression		χ^2	*P*
		Low (*n*=30)	High (*n*=30)		
Gender				0.024 4	0.875 8
Male	45	29	16		
Female	15	10	5		
Age				0.230 7	0.631 0
≥50	25	12	13		
<50	35	19	16		
EBV-VCA IgA (SU)				5.275	0.021 6
≥20	38	11	27		
<20	22	13	9		
Size/cm				4.667	0.030 8
≤6	51	36	15		
>6	9	3	6		
Metastasis				7.516	0.006 1
Yes	46	14	32		
No	14	10	4		

SU: standard units.

2.3 The expression of MUC1 was knocked down in the NPC cells

Based on relationship between MUC1 expression and size of tumor in the patients with NPC, the NPC cells were used to investigate the regulation mechanism of MUC1. The expression of MUC1 was measured in the normal human nasopharyngeal epithelial cells and NPC cells. Figure 2a showed that the expression of MUC1 mRNA was upregulated in the NPC cells, such as CNE1, 5-8F and HNE1 compared with that in NP69 cells. Based on the high expression of MUC1 mRNA in NPC cells, the 5-8F and HNE1 cells were used for the further study. The 5-8F and HNE1 cells were transfected with si-control and si-MUC1, and then the expression of MUC1 mRNA was analyzed by qPCR. The expression of MUC1 mRNA in the cells transfected with si-control was same as that in the 5-8F cells and HNE1, and the expression of MUC1 was significantly down-regulated in the si-MUC1 cells compared with that in the si-control cells (Figure 2b, e). Results of MUC1 protein was consistent with that of MUC1 mRNA, which suggested that MUC1 was successfully knocked-down by si-MUC1 in the 5-8F (Figure 2c, d) and HNE1 (Figure 2f, g) cells.

2.4 Knock−down of MUC1 inhibited the proliferation， promoted the apoptosis in the NPC cells

To investigate the effect of MUC1 on malignant characteristics of NPC cells, the proliferation was analyzed by CCK-8 and colony formation assay, and apoptosis was analyzed by flow cytometry. The result showed that *A* value of cells transfected si-control was same as that of 5-8F cells in indicative time, whereas *A* value of cells transfected si-MUC1 was significantly lower than that of cells transfected with si-control at 36 h and 48 h (Figure 3a). The colonies of cells with si-control were same as that of 5-8F, while the colonies of cells with si-MUC1 were significantly fewer than that of cells with si-control (Figure 3b, c). The proliferation of HNE1 with si-MUC1 was similar to that of 5-8F cells with si-MUC1 (Figure 3f–h). These results suggested that knock-down of MUC1 decelerated the proliferation of NPC cells.

The apoptosis of cells was analyzed by flow cytometry. Apoptosis of cells transfected with si-control was almost consistent with apoptosis of NPC, while the apoptosis of cells transfected with si-MUC1 was increased compared with that of cells

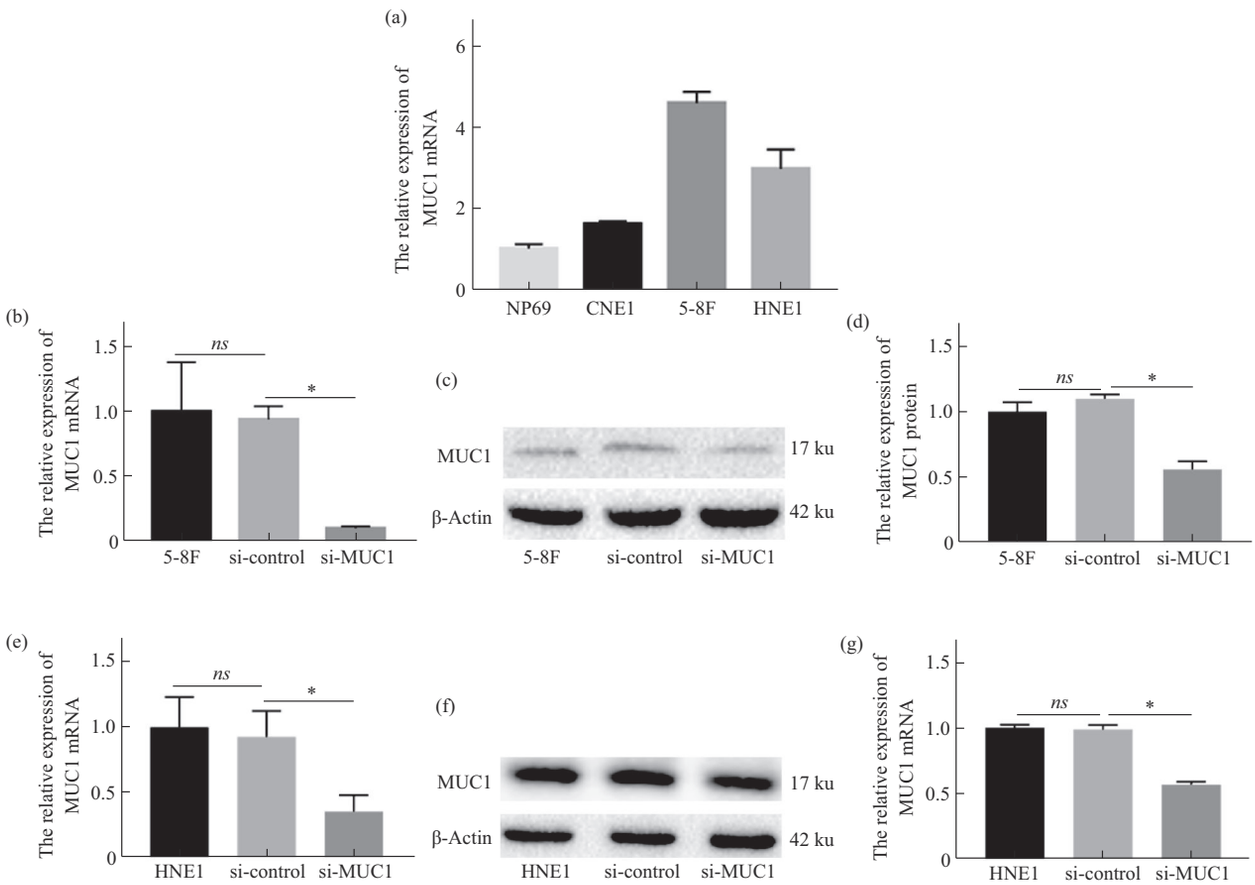

Fig. 2 MUC1 was knocked down by si−MUC1 in the NPC cells

The expression of MUC1 mRNA was detected by qPCR in normal human nasopharyngeal epithelial cells (NP69) and NPC cells (CNE1, 5-8F, HNE1) (a) . The 5-8F and HNE1 cells were transfected with si-control and si-MUC1, then, the expression of MUC1 mRNA was analyzed by qPCR in 5-8F (b) and HNE1 cells (e). The expression of MUC1 protein was analyzed by Western blot in the transfected 5-8F (c, d) and HNE1 (f, g) cells. *ns*, $P>0.05$, *$P<0.05$, Tukey's multiple comparisons of two-way ANOVA.

transfected with si-control in the 5-8F (Figure 3d, e) and HNE1 cells (Figure 3i, j), which suggested that downregulation of MUC1 promoted the apoptosis of NPC cells.

2.5 Downregulation of MUC1 regulated the proliferation and apoptosis by inactivating NF−κB signaling pathway in the NPC cells

Above results showed that downregulation of MUC1 inhibited that proliferation, and promoted the apoptosis. To explore the underly mechanism of MUC1 on regulate characteristics of malignancy in the NPC cells, the proteins of NF-κB signaling pathway and inflammatory factors were measured in the 5-8F cells transfected with si-MUC1. As shown in Figure 4a, the TNF-α and IL-6 mRNA levels in the si-control cells was the same as that in the 5-8F cells, but the TNF-α and IL-6 levels in the si-MUC1 cells transfected were decreased compared with that in the si-control cells. The results of TNF-α and IL-6 proteins were consistent with the result of corresponding mRNAs (Figure 4b). The Figure 4c, d had shown that the phosphorylated- (p-) IκB and p-P65 proteins levels in the si-control cells were the same as that in the 5-8F cells, however, p-IκB and p-P65 were downregulated in si-MUC1 cells compared with that in the si-control cells. The Bax/Bcl-2 ratio of si-control cells was lower than that of 5-8F cells, whereas, Bax/Bcl-2 ratio of the si-MUC1 cells was significantly higher than that of si-control cells.

Combined with the above results, it is testified the downregulation of MUC1 could inhibit the proliferation and promote apoptosis by inactivating NF-κB signaling pathway in the NPC cells.

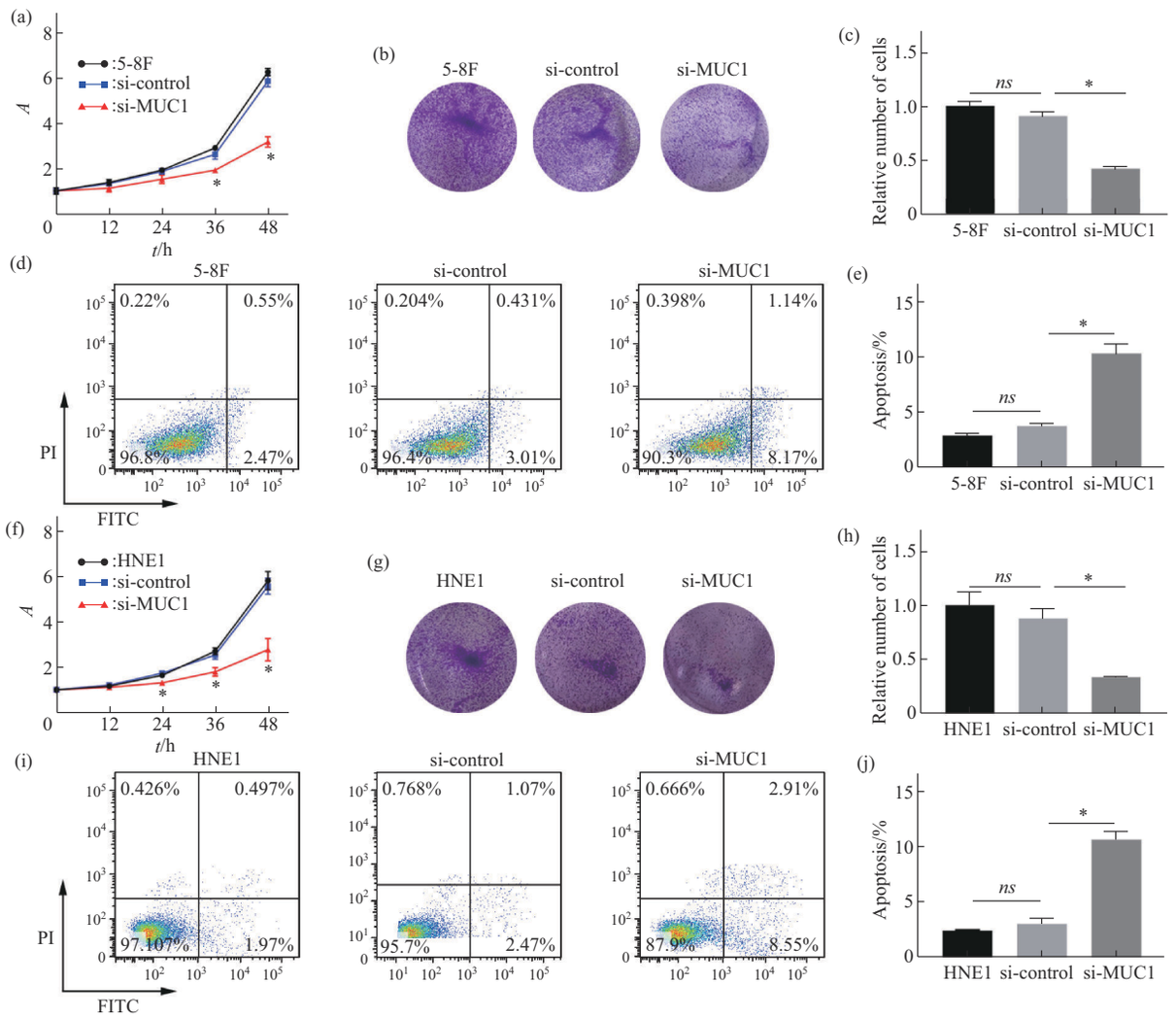

Fig. 3　Downregulation of MUC1 inhibited the proliferation, promoted the apoptosis in the NPC cells

The 5-8F and HNE1 cells were transfected with si-control or si-MUC1. The CCK-8 assay was executed to analyze the proliferation of cells on the indicated time in 5-8F (a) and HNE1 (f) cells. The colony formation assay was used to analyze the proliferation of 5-8F (b, c) and HNE1 (g, h) cells. The CCK-8 and colony farmation assays showed that downregulation of MUC1 inhibited the proliferation in the NPC cells. Flow cytometry assay showed that apoptosis of si-MUC1 cells was increased compared with that of si-control, which downregulation of MUC1 accelerated apoptosis of 5-8F (d, e) and HNE1 cells (i, j). All data were represented *mean*±*SD* from three independent experiments. *ns*, $P>0.05$, *$P<0.05$, Tukey's multiple comparisons of two-way ANOVA.

3　Discussion

NPC was a malignant epithelial carcinoma of head and neck, and had a relatively high incidence in China[6-7]. It was showed that EBV infection and inflammation accelerated the progress of NPC[2-3]. A research showed that NOTCH2 was down-regulated in the patients with NPC; meanwhile, knock-down of NOTCH2 could promote metastasis by EMT in NPC[21]. The expression of miR-9 was decreased in the NPC tissues, and it was verified that exosomal miR-9 suppressed angiogenesis by directly targeting MDK and regulating PDK/AKT pathway in the NPC[22]. The expression of histone deacetylase 4 (HDAC4) was significantly increased in the primary and metastatic NPC tissues and high HDAC4 expression predicted a poor overall survival (OS) of NPC patients[23]. lncRNA SNHG6 accelerated progression of NPC *via* regulating miR-26a-5p/ARPP19 signal axis[24]. MiR-335 methylation was higher in the NPC tissues, which was correlated with metastasis of NPC[25]. Thus, it could be seen that

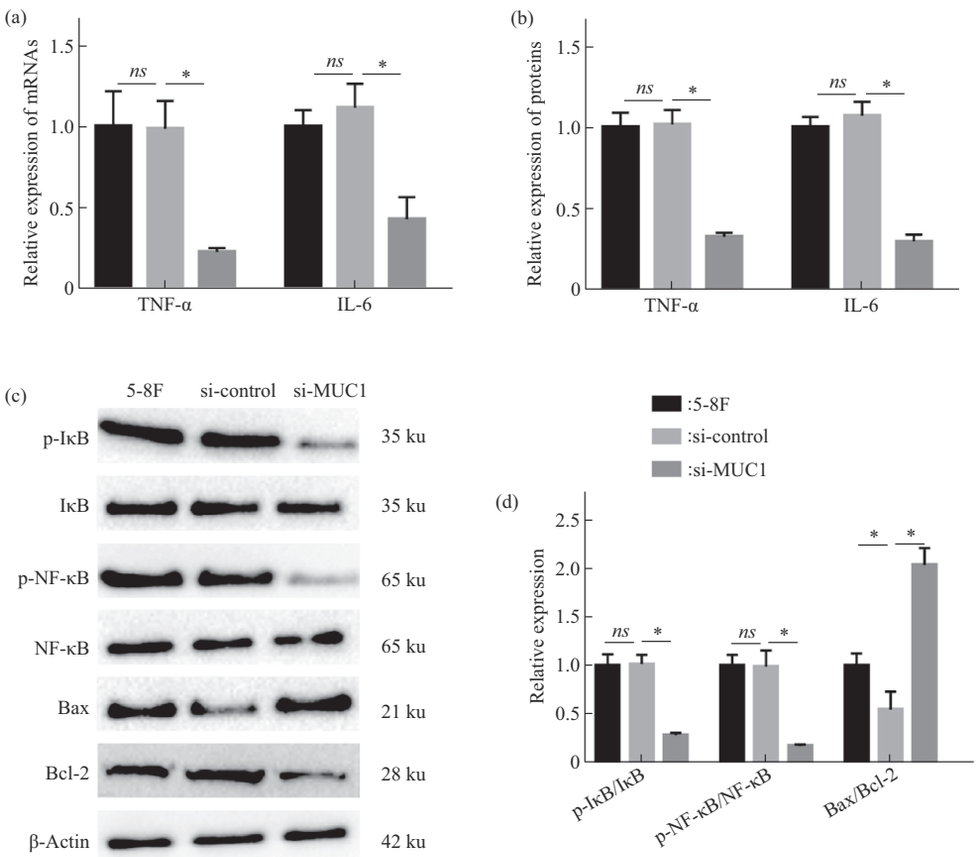

Fig. 4 Silencing of MUC1 inhibited the expression of inflammatory factors by inactivating NF−κB pathway, and regulated the expression of apoptosis−related proteins in the NPC cells

The 5-8F cells transfected with or without si-MUC1. The expression of TNF-α and IL-6 mRNAs (a) and proteins (b) were respectively analyzed by qPCR and ELISA. The indicated proteins were visualized by Western blot (c). The expression of p-IκB/IκB, p-NF-κB/NF-κB and Bax/Bcl-2 were analyzed in the transfected 5-8F cells (d). All data were represented *mean*±*SD* from three independent experiments. *ns*, $P>0.05$, *$P<0.05$, Tukey's multiple comparisons of two-way ANOVA.

disorders of multiple genes and signaling pathways accelerated the progress of NPC by regulating the malignant characteristics of cells.

MUC1 was expressed on the apical surface of epithelial cells in many different tissues including lung, breast, stomach, pancreas, *etc*. And the MUC1 could form protective mucous barriers. Aberrant expression of MUC1 was associated with cancers. It was confirmed that upregulation of MUC1 was one of biomarkers for prognosis and drug resistance of bladder cancer[26] and prostate cancer[27]. The score of MUC1 staining was increased in the oral squamous cell carcinoma compared with oral epithelium of normal and oral epithelial dysplasia[28]. MUC1 was overexpressed in the breast cancer, and it had been shown that MUC1 was an effective target for breast cancer chemotherapy[29-30]. In this study, it was confirmed the expressions of MUC1 mRNA and protein were upregulated in the patients with NPC, which was consistent with previous research that abnormal expression of MUC1 was associated with NPC[16]. Meanwhile, our results showed the high expression of MUC1 contributed to growth of NPC by analyzing relationship between MUC1 expression and clinicopathological variables. To clarify the influence of MUC1 on malignant biological characteristics of NPC, proliferation and apoptosis were analyzed. The results had suggested that the proliferation was retarded and apoptosis was accelerated in NPC cells with knock-down of MUC1. In other words, the MUC1 could aggravate the malignant characteristics of NPC cells, which was consistent with the role of

MUC1 in a variety of cancers, such as clear cell renal cell carcinoma[31], osteosarcoma[32] and hepatocellular carcinoma cells[33].

A large number of genes were differentially expressed in NPC, which were enriched in NF-κB signaling pathway[34]. EBV-encoded LMP1 expression underpinned NF-κB activation in NPC[35]. The NKILA repressed NPC carcinogenesis and metastasis by inhibiting NF-κB pathway[36]. Overexpression of SIRT6 induced apoptosis of NPC cells by inactivating NF-κB signaling[37]. AKR1B10 was increased in the NPC with radiotherapy resistance, and overexpression of AKR1B10 stimulated proliferation, suppressed apoptosis and decreased NPC cellular DNA damage after radiotherapy by activating FFA/TLR4/NF-κB axis in the NPC cells[38]. Cancer-associated fibroblasts induced the formation of radioresistance and promoted NPC cell survival following irradiation *via* the IL-8/NF-κB pathway to reduce irradiation-induced DNA damage[39]. Ginkgolic acid suppressed growth of NPC cells by inhibiting NF-κB[40]. Simvastatin induced apoptosis of NPC cells through inactivating NF-κB signaling pathway[41]. Thus, NF-κB signaling pathway played a critical role in progress of NPC, and was one of the target genes for treatment of NPC.

There were increasing evidences that NF-κB signaling pathway was overactivated by MUC1 in a variety of cancers[17-18, 42], except for NPC. There was no doubt that TNF-α and IL-6 was inflammatory factors regulated by NF-κB signaling pathway[43]. The relationship analysis showed that the expression of MUC1 was positively correlated with EBV infection. EBV infection accelerated the process of NPC by stimulating inflammatory response[44]. It was verified that down-regulated of MUC1 decreased the expression of TNF-α, IL-6, p-IκB, p-NF-κB, Bax and Bcl-2, which implied that down-regulated of MUC1 could inactivate the NF-κB. Combined with the effect of NF-κB on biological behavior of cancer cells and our results that loss of MUC1 inhibited proliferation, induced apoptosis of NPC cells, we speculated that knockdown of MUC1 could weaken malignant features of NPC cells through abolishing the activity of NF-κB in the NPC cells.

4 Conclusion

In this study, we had verified that MUC1 was highly expressed in the NPC patients. The MUC1 expression was positively correlation with EBV infection. And the high expression of MUC1 was prone to metastasis of NPC. Functionally, downregulation of MUC1 significantly inhibited the proliferation and induced the apoptosis. Mechanically, the reduction of MUC1 dramatically reduced the expression of TNF-α and IL-6, inhibited the phosphorylation of IκB and NF-κB, and regulated the expressions of Bax and Bcl-2. In conclusion, loss of MUC1 significantly suppressed the proliferation, promoted apoptosis by inactivating NF-κB signaling pathway. However, there are some limitations as follows. First, knockdown of MUC1 inhibited malignant characteristics of NPC cells *in vitro*. Further study still is executed to verify the inhibitor of MUC1 on the malignant characteristics *in vivo*. Second, the specific mechanism of how MUC1 inhibits malignant features of NPC cell by regulating NF-κB signaling pathway remains to be further explored.

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MUC1下调通过失活NF-κB通路抑制鼻咽癌细胞增殖并促进其凋亡*

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摘要　目的　为了探讨黏蛋白1（MUC1）对鼻咽癌（nasopharyngeal carcinoma，NPC）细胞增殖与凋亡的影响及其调控机制。**方法**　收集泉州市第一医院2020年10月~2021年7月60例NPC及配对癌旁正常组织。采用实时定量PCR（real-time quantitative PCR）检测MUC1在NPC患者中的表达。将对照siRNA或靶向*MUC1*的siRNA（si-MUC1）转染5-8F和HNE1细胞。分别用CCK-8和集落形成实验分析5-8F和HNE1细胞的增殖，流式细胞术分析5-8F和HNE1凋亡情况；qPCR和ELISA检测TNF-α和IL-6水平；Western blot检测MUC1、NF-κB及凋亡相关蛋白的表达。**结果**　MUC1在NPC组织中表达上调；MUC1高表达的NPC患者易发生EBV感染、NPC增长和转移；MUC1的缺失抑制了NPC细胞的增殖和凋亡等恶性生物学行为，下调p-IκB、p-P65和Bcl-2的表达，上调Bax的表达。**结论**　MUC1下调可通过失活NF-κB信号通路抑制NPC恶性生物学行为。

关键词　黏蛋白1，鼻咽癌，NF-κB信号通路，增殖，凋亡
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