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Original Article

LncRNA SNHG5 promotes the invasion and proliferation of oropharyngeal squamous cell carcinoma by regulating the miR-21/PTEN signaling pathway

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Abstract: Objective: To delineate the functional role of long non-coding RNA (LncRNA) SNHG5 in oropharyngeal squamous cell carcinoma (OPSCC). Methods: The expression of LncRNA SNHG5 in paired tumor/adjacent tissues and cell lines (HN6 vs. HIOEC) were detected, and the relationship between LncRNA SNHG5 expression in cancer tissues and the clinicopathological characteristics and prognosis of patients was analyzed. The functional characterization including proliferation, expression of LncRNA SNHG5, miR-21, PTEN, VEGF, MMP-9, cell invasion, as well as cell apoptosis were detected in siRNA-mediated SNHG5 knockdown in HN6 cells. Results: Tumor tissues exhibited higher SNHG5 expression versus adjacent mucosa (P<0.001). Elevated SNHG5 positively correlated with advanced TNM staging, lymph node metastasis, and poor differentiation (P<0.05). Patients with high SNHG5 showed significantly reduced 5-year overall survival (P=0.035). SNHG5 silencing decreased proliferation and invasion capacity, while increasing apoptosis. Mechanistically, SNHG5 knockdown downregulated oncogenic miR-2, VEGF, and MMP-9, while restoring tumor-suppressive PTEN expression. Conclusion: Our findings suggest SNHG5 is a master oncogenic regulator in OPSCC that mechanistically promotes tumor progression via miR-21/PTEN pathway activation. The strong association between SNHG5 overexpression and adverse clinicopathological features, coupled with its prognostic independence, positions this lncRNA as a promising therapeutic target and molecular stratification biomarker.

Keywords: LncRNA SNHG5, miR-21/PTEN signaling pathway, oropharyngeal squamous cell carcinoma

Introduction

Oropharyngeal squamous cell carcinoma (OPSCC) represents a highly aggressive epithelial malignancy constituting over 90% of oropharyngeal cancers, with squamous cell histology accounting for 7.4% of all head and neck neoplasms [1, 2]. The anatomically complex location of these tumors, coupled with their propensity for early lymphatic dissemination and therapeutic resistance, contributes to dismal 5-year survival rates of 15%-25% in advanced-stage patients [3, 4]. Notably, over 50% of cases present with locally advanced or metastatic disease at diagnosis, a clinical challenge exacerbated by the absence of reliable early detection biomarkers [4]. These persistent clinical hurdles underscore the urgent need to decipher the molecular drivers of OPSCC pathogenesis for developing novel therapeutic strategies.

Long non-coding RNAs (lncRNAs), defined as transcripts exceeding 200 nucleotides with limited protein-coding potential, have emerged as pivotal regulators in carcinogenesis through diverse mechanisms including chromatin remodeling and post-transcriptional modulation [5, 6]. Of particular interest, small nucleolar RNA host gene 5 (SNHG5) has recently gained attention for its oncogenic roles across multiple malignancies. Mechanistic studies reveal that SNHG5 functions as a competitive endogenous RNA (ceRNA) by sequestering

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tumor-suppressive miRNAs - for instance, its sponging of miR-155 enhances melanoma progression via apoptosis inhibition [7, 8]. This 524-nucleotide transcript, processed from the snoRNA U50/U50' host gene, resides at chromosomal breakpoint clusters implicated in genomic instability [6]. While accumulating evidence implicates SNHG5 dysregulation in gastrointestinal and breast carcinogenesis [9, 10], its functional repertoire in OPSCC remains uncharted territory.

Building upon these insights, we hypothesize that SNHG5 may orchestrate OPSCC progression through miRNA-mediated signaling networks. This study pioneers the investigation of SNHG5-mediated ceRNA crosstalk in OPSCC, specifically interrogating its regulatory effects on the miR-21/PTEN axis - a pathway critically involved in epithelial-mesenchymal transition and metastatic dissemination. Through integrated clinical and experimental approaches, we aim to establish SNHG5 as both a mechanistic driver and therapeutic vulnerability in OPSCC pathogenesis.

Materials and methods

Materials

A prospective cohort of 86 treatment-naïve OPSCC patients undergoing surgical resection at the Second Affiliated Hospital of Chengdu Medical College (March 2018-December 2021) was enrolled. Paired tumor specimens and histologically normal adjacent tissues (collected ≥5 cm from tumor margins) were cryopreserved in liquid nitrogen within 15 min post-resection and stored at -80°C. Exclusion criteria included prior radiotherapy, chemotherapy, or immunotherapy. Postoperative follow-up (median 32 months; range 12-60 months) utilized multimodal tracking including clinic visits, telemedicine consultations, and electronic health records, with overall survival as the primary endpoint (cutoff: December 2024). The study protocol adhered to the Declaration of Helsinki principles, with written informed consent obtained from all participants or their legal guardians.

Cell culture

The human OPSCC HN6 cell line and the immortalized oral epithelial cell line HIOEC were both purchased from the American Type Culture Collection (ATCC). HN6 and HIOEC cells were maintained in DMEM (Hyclone Corporation, USA) supplemented with 10% FBS (GBICO, USA) under standard conditions (37°C, 5% CO_2). Subculturing was performed at 80-90% confluence using 0.25% trypsin-EDTA (Hyclone, Inc.). Cells with Mycoplasma contamination were routinely excluded using PCR-based testing.

Transfection of cells

HN6 cells in the logarithmic growth phase were trypsinized and seeded into 6-well plates at a density of 5×10^5 cells/well. Transfection was initiated when cells reached 80-90% confluence. The SNHG5 overexpression construct (pcDNA3.1-SNHG5) and empty vector control (pcDNA3.1+) were generated by subcloning the full-length SNHG5 cDNA (GenBank: XR_001738.1) into the pcDNA3.1(+) backbone (Invitrogen, Carlsbad, CA, USA). Transient transfection was performed using Lipofectamine 2000 (Invitrogen, USA). After 6 hours of transfection, the medium was replaced with fresh complete medium containing 10% fetal bovine serum, and cells were maintained for 48 hours prior to functional assays. siRNA (si-SNHG5: 5'-AAGCTTCTTTTACGTCGGCCTTCGCGAGCGTCTGG-3') and scrambled negative control siRNA (si-NC: 5'-CCAGACTGCAGGTTTGAC-3') were synthesized by Shanghai GenePharma Co., Ltd., China. Untransfected cells served as the blank control group. Additional experimental groups included cells transfected with miR-21 inhibitor (antagomiR-21: 5'-CCGGTCAACATCAGTCTGATAAGCTATTTTTG-3') and its negative control (miR-NC: 5'-AATTCAAAAATAGCTTATCAGACTGATGTTGA-3'; both from Shanghai GenePharma).

Detection of RNA by qRT-PCR

The total RNA was extracted from the sample with Trizol reagent (Invitrogeng, Inc., USA), and reverse-transcribed into cDNA as per the instructions of the reverse transcription kit (Takara, Japan). The reaction system was 20 μL, and the reaction conditions were 37°C for 15 min and 85°C for 5 s. SYBR Premix Ex Taq kit (Japan TOYYOBO company) was used to amplify cDNA synthesis, and qRT-PCR reaction was performed by real-time fluorescence quantitative PCR (7900HT fluorescence quantitative

Table 1. Primer sequences

Primer		Sequence (5'-3')
NHG5	Forward primer	TAGAGATGCAAAGATACACGAAA
	Reverse primer	CACACTCAGAACGATGTTCAC
miR-21	Forward primer	AGTGTCCAGCTCGGTAGCTTATGACA
	Reverse primer	GGCTGTGGTCCAGTGCC
PTEN	Forward primer	GACCTTGGCAAGGTCGACTG
	Reverse primer	ACCCTATGGCTGGTCACTCAGTTCA
VEGF	Forward primer	AGGGCAGAATCATCACGAAGT
	Reverse primer	AGGGTCTCGATTGGATGGCA
MMP-9	Forward primer	TGTACCGCTATGGTTACACTCG
	Reverse primer	GGCAGGGACGAAGCCTTG
GAPDH	Forward primer	GGAGCCAGATCCCTCCAAAAT
	Reverse primer	GTGCAGGGTGAGCT
U6	Forward primer	GCGCGTCGTGAAGCGTTC
	Reverse primer	GTGCAGGGTCCGAGG

PCR, ABI, USA). The qRT-PCR reaction conditions were 95°C for 5 min, 95°C for 15 s, 58°C for 30 s, 74°C for 30 s, with a total of 40 rounds. GAPDH and U6 (internal reference of miR-21) were used as internal reference genes, and the relative expression of the target gene was calculated by the $2^{-\Delta\Delta Ct}$. The primers were synthesized by Shanghai Sangon Biotech Co., Ltd. with the sequence of primers listed in **Table 1**.

Detection of cell proliferation activity by MTT

Transfected cells were seeded in 96-well plates (1×10^4 cells/well). At 12, 24, 48, and 72 h, the medium was replaced with 10 μL MTT solution (MTT Kit, Shanghai Yinxue Biology). After 4 h incubation, formazan crystals were dissolved in 100 μL DMSO, and absorbance was measured at 450 nm by a Multi-functional microplate reader (Perkin Elmer, USA). Each group included five technical replicates, with experiments repeated three times independently.

Detection of protein expression by Western blot

The total protein in cells was extracted with RIPA lysis buffer that contained PMSF. The cells were incubated on ice for 30 min, and centrifuged for 5 min (1000 g, 4°C) to extract the supernatant. The BCA protein analysis kit (Shanghai Beyotime Biotechnology) was applied to quantitatively analyze the protein concentration, the protein was separated by 10% SDS-PAGE gel electrophoresis, transferred to a PVDF membrane, and blocked with 5% skimmed milk powder at room temperature for 2 h. Membranes were incubated overnight at 4°C with primary antibodies: PTEN (1:1000; Abcam #ab32199), VEGF (1:2000; Abcam #ab52917), MMP-9 (1:1500; Abcam #ab76003), and β-actin (1:1000; Beyotime #AA128). After Goat Anti-Mouse IgG/HRP secondary antibody (1:5000; Beijing Zhongshan Golden Bridge Biotechnology Co., Ltd.) incubation, signals were detected using ECL Plus (Millipore #WBKLS0500) and quantified with Image Lab 3.0 (Bio-Rad).

Detection of cell invasion by Transwell assay

Matrigel-coated Transwell inserts (CoStar, USA) were hydrated with serum-free DMEM. Cells (5×10^4/well) in 200 μL serum-free medium were added to the upper chamber, while the lower chamber contained 600 μL medium with 10% FBS. After 24 h, invading cells were fixed with 4% paraformaldehyde, stained with 0.1% crystal violet (Sigma #C0775), and imaged under an IX53 inverted microscope (Olympus, Japan). Five random fields were counted per insert.

Apoptosis experiment

Cells (2×10^5/well) were harvested and stained with Annexin V-FITC/PI (BD Biosciences #556547) per manufacturer guidelines. Samples were analyzed on a Falcon Flow Cytometer (BD, USA) within 1 h.

Dual-luciferase reporter gene assay

The 3'-UTR of SNHG5 containing putative miR-21 binding sites was cloned into pmirGLO (Promega #E1330) to generate pmirGLO-SNHG5-WT. A mutant construct (pmirGLO-SNHG5-Mut) was generated using a Site-Directed Mutagenesis Kit (Takara #639649). HN6 cells were co-transfected with 50 nM miR-21 mimic (Dharmacon #C-300592-05) or antagomiR-21 (Dharmacon #IH-300592-08) and 100 ng reporter plasmid. Renilla/Firefly luciferase activity was measured after 48 h using the Dual-Luciferase Kit (Promega #E1910).

Statistical analysis

Statistical software SPSS 23.0 was adopted for data processing and analysis. Data are pre-

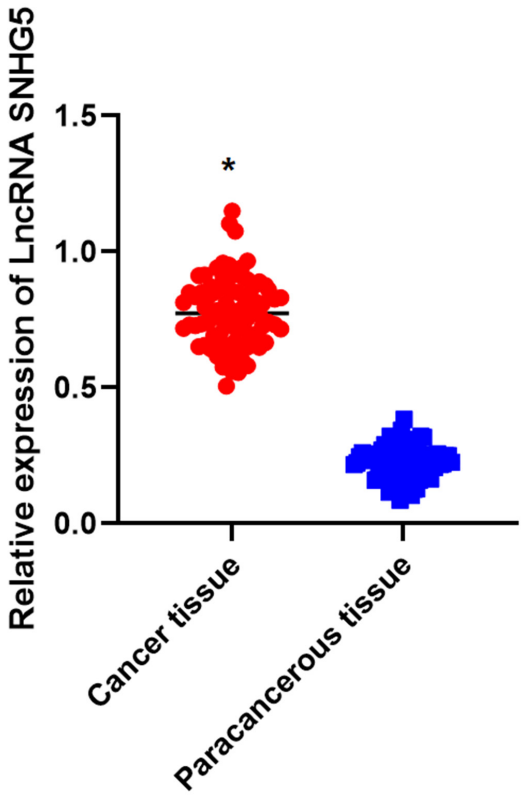

Figure 1. LncRNA SNHG5 expressions in cancer tissues and paracancerous tissues. Compared with paracancerous tissues, **P<0.05.*

sented as mean±SD from three independent experiments. Comparisons used Student's t-test (two groups) or ANOVA with Tukey's post hoc test (multiple groups). Categorical variables were expressed in percentage (%), and analyzed by Chi-square test. Survival curves were generated via the Kaplan-Meier method and compared by log-rank test. Multivariate analysis employed Cox proportional hazards regression. P<0.05 was considered statistically significant.

Results

Differential expression of SNHG5 in tumor vs. adjacent tissues

Tumor tissues exhibited higher SNHG5 expression compared to matched adjacent normal tissues (t=57.281, P<0.001; **Figure 1**), as quantified by qRT-PCR.

Clinicopathological correlations of SNHG5 overexpression

Elevated SNHG5 levels strongly correlated with advanced TNM stage (t=6.984, P<0.001), lymph node metastasis (t=7.173, P<0.001), and poor tumor differentiation (t=4.469, P< 0.001). No associations were observed with gender, age, or tumor location (P>0.05; **Figure 2**).

Prognostic significance of SNHG5 expression

Using median expression (0.736) as the cutoff, high SNHG5 expression patients demonstrated significantly reduced 5-year overall survival (P=0.035; **Figure 3**).

Key prognostic factors analyzed by univariate analysis and multivariate cox regression model analysis

We performed Univariate Analysis and multivariate Cox regression model analysis to analyze the factors that may affect the survival and prognosis of patients, and the results showed that TNM stage III-IV, high LncRNA SNHG5 expression and lymph node metastasis were independent predictors of poor prognosis (**Tables 2** and **3**).

Expression of LncRNA SNHG5 in HN6 and HIOEC cell models

The relative expression of LncRNA SNHG5 in human OPSCC HN6 cells was dramatically higher than that of oral epithelial cell line HIOEC (t=18.437, P<0.001; **Figure 4**).

Functional consequences of SNHG5 silencing

After transfection, the relative expression of LncRNA SNHG5 were successfully silenced by siRNA-SNHG5 (**Figure 5A**). After transfection for 24 h, 48 h and 72 h, the absorbance value at 450 nm, the number of invading cells in the siRNA-SNHG5 group was apparently lower than that in the siRNA-NC group and control group, while the apoptotic rate was significantly higher (*P<0.05*). However, the measures between the siRNA-NC group and control group were not statistically significant at each time point (*P>0.05*) (**Figure 5B-D**).

Comparison of the transfected miR-21/PTEN signaling expression in each group

Dual-luciferase reporter assays demonstrated that miR-21 overexpression significantly reduced the luciferase activity of the wild-type SNHG5 construct (WT: 0.52±0.07 vs. NC: 1.02± 0.08; P<0.05), while showing no inhibitory

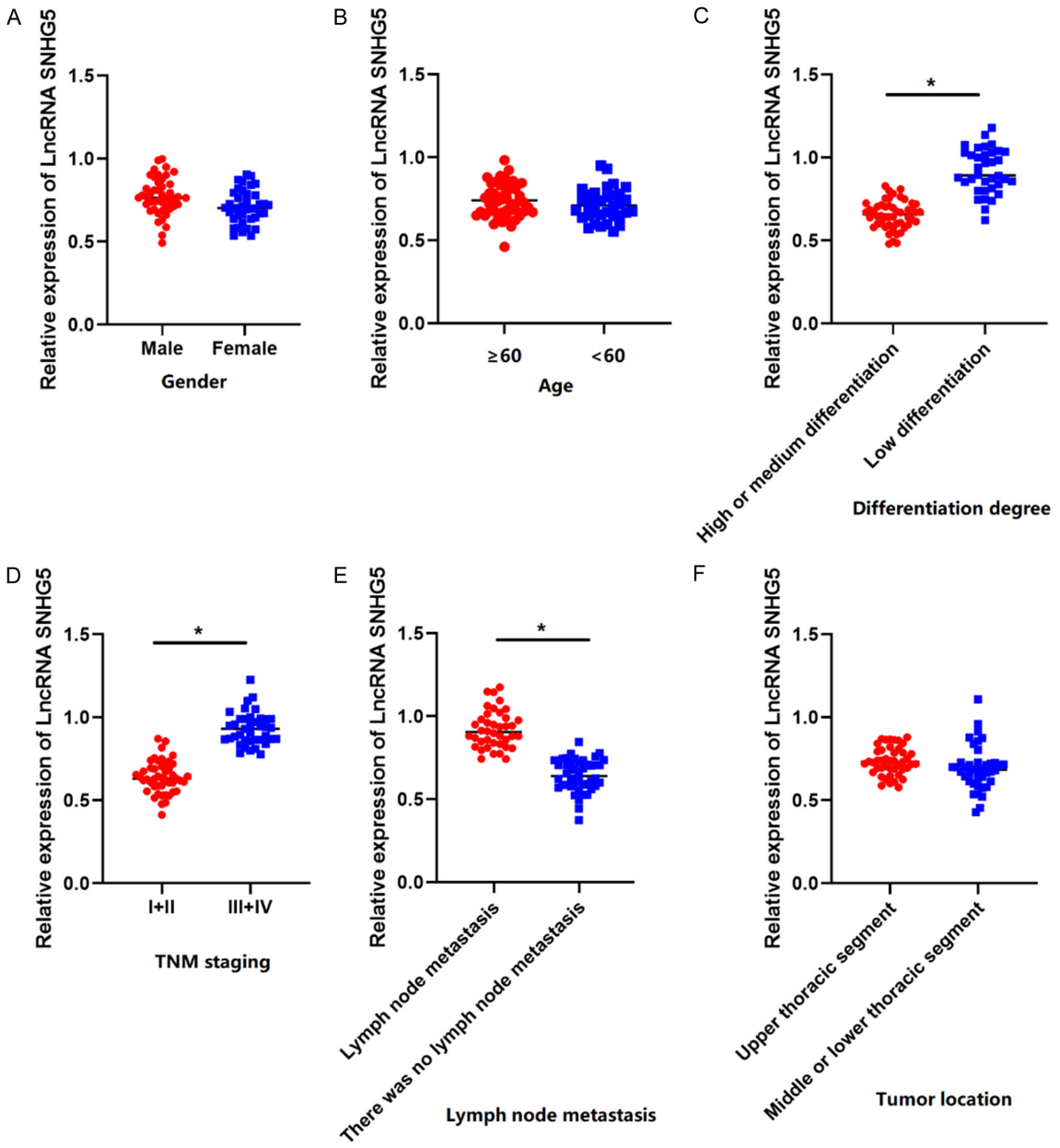

Figure 2. The connection between the LncRNA SNHG5 expression and the clinicopathological characteristics of patients with oropharyngeal squamous cell carcinoma. **P<0.05.*

effect on the mutant (Mut: 0.98±0.11 vs. NC: 1.02±0.08; P>0.05). Conversely, miR-21 inhibition markedly enhanced SNHG5-WT reporter activity (2.17±0.26 vs. NC: 1.08±0.09; P<0.05), with no significant changes observed in the mutant group (Mut: 0.99±0.10 vs. NC: 1.08±0.09; P>0.05) (**Figure 6A**).

After transfection, the expressions of miR-21, VEGF mRNA, protein VEGF, MMP-9 mRNA and protein MMP-9 in the siRNA-SNHG5 group were remarkably lower than in the siRNA-NC group and control group (*P<0.05*). The expressions of PTEN mRNA and PTEN protein in the siRNA-SNHG5 group were dramatically higher than that in the siRNA-NC group and control group (*P<0.05*), and the difference in protein comparison between the siRNA-NC group and control group was not statistically significant (*P>0.05*) (**Figure 6B** and **6C**).

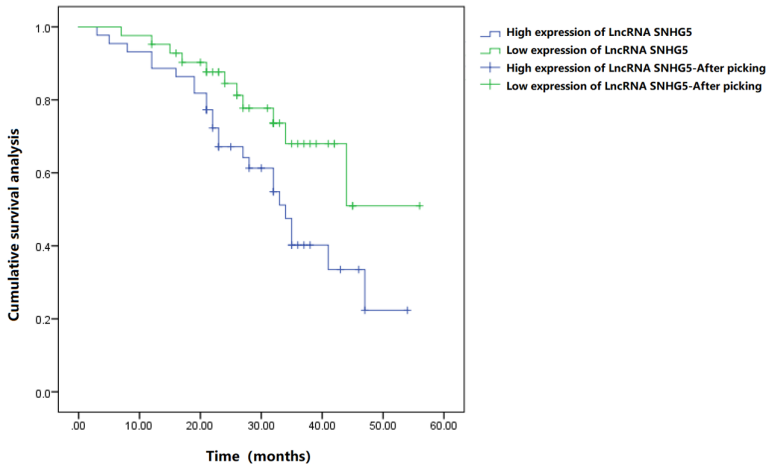

Figure 3. Relationship between LncRNA SNHG5 expression and clinical prognosis in oropharyngeal squamous cell carcinoma.

Effect of miR-21 inhibitor on SNHG5 expression

miR-21 inhibition could significantly suppress the expression of miR-21 in NH6 cells, and the expression of SNHG5 was also decreased (*P<0.05*) (**Figure 7**).

Discussion

Oropharyngeal carcinoma represents a significant global health burden, characterized by notably high incidence and mortality rates in China. As one of the most lethal malignancies worldwide, its insidious onset poses diagnostic challenges. Early-stage symptoms are often nonspecific, manifesting as mild pharyngeal discomfort or persistent globus sensation, which frequently leads to delayed clinical detection. Consequently, over 60% of patients are diagnosed at mid-to-advanced stages [11]. As the disease progresses, patients typically develop odynophagia (painful swallowing) with referred otalgia. Advanced stages present with hallmark clinical features including blood-tinged saliva, halitosis, and progressive dyspnea. Tumor enlargement frequently causes dysphagia and upper airway obstruction, necessitating emergent interventions. Notably, the aggressive nature of this malignancy is underscored by its propensity for local relapse and distant metastasis, which collectively drives poor prognosis and contributes to elevated mortality rates. These biological behaviors also impose substantial therapeutic challenges, often rendering conventional treatment modalities less effective [12].

Emerging evidence has established that lncRNAs participate in diverse biological processes and are critically implicated in the pathogenesis of various diseases. The initial identification of AFAP1-AS1 (a lncRNA transcribed from the antisense strand of the *AFAP1* gene encoding actin filament-associated protein 1) as a differentially expressed transcript in esophageal adenocarcinoma has catalyzed extensive research into tumor-associated lncRNAs [13, 14]. Notably, multiple lncRNAs exhibit differential expression patterns between OPSCC tissues and adjacent normal mucosa, suggesting their potential regulatory roles in tumor initiation and progression [15, 16]. Of particular interest is small nucleolar RNA host gene 5 (*SNHG5*), a chromatin-associated lncRNA localized at chromosome 6q14.3. Emerging evidence positions *SNHG5* as a putative oncogenic driver [12]. Its functional significance is further underscored by radiation-responsive expression dynamics: significant alterations in *SNHG5* levels have been observed not only in X-ray-irradiated TK6 lymphoblastoid cells but also in neighboring non-irradiated bystander cells [17-19], implying potential involvement in radiation-induced genomic instability. Our clinicopathological analysis revealed three key findings: firstly, *SNHG5* expression was markedly elevated in tumor tissues compared to matched adjacent normal tissues; secondly, elevated *SNHG5* levels correlated significantly with advanced TNM staging, lymph node metastasis, and poor tumor differentiation; thirdly, patients with low *SNHG5* expression demonstrated superior 5-year overall survival compared to high expressors. These findings align with prior reports of *SNHG5* overexpression in esophageal squamous cell carcinoma and extend its oncogenic relevance to esophageal squamous cell carcinoma [20-22]. The consistent association between *SNHG5* upregulation and aggressive tumor phenotypes across multiple malignancies strongly suggests its fundamental role in regulating

Table 2. Univariate analysis of prognostic influencing factors

Factor	n	Five-year survival rate (%)	χ^2	P
Gender				
Male	45	40.00	0.315	0.575
Female	41	34.15		
Age				
≥60 years	37	15 (40.54)	0.308	0.579
<60 years	49	17 (34.69)		
Degree of tumor differentiation				
Moderately and well differentiated	61	26 (42.62)	2.632	0.105
Poorly differentiated	25	6 (24.00)		
TNM staging				
I+II	52	27 (51.92)	12.188	0.001
III+IV	34	5 (14.71)		
Lymph node metastasis				
Yes	38	6 (15.79)	12.786	0.000
No	49	26 (53.06)		
The expression of LncRNA SNHG5				
High expression	45	8 (17.78)	15.254	0.000
Low expression	41	24 (58.54)		

Table 3. Multivariate Cox model analysis of the crucial factors that may affect patients' prognosis

Factors	β	SE	Wald	P	OR	95% CI
TNM stage III-IV	0.982	0.421	8.162	0.001	2.894	1.281-5.432
High LncRNA SNHG5 expression	0.683	0.321	6.595	0.015	2.216	1.373-4.783
Lymph node metastasis	0.622	0.303	5.075	0.029	2.095	1.511-4.352

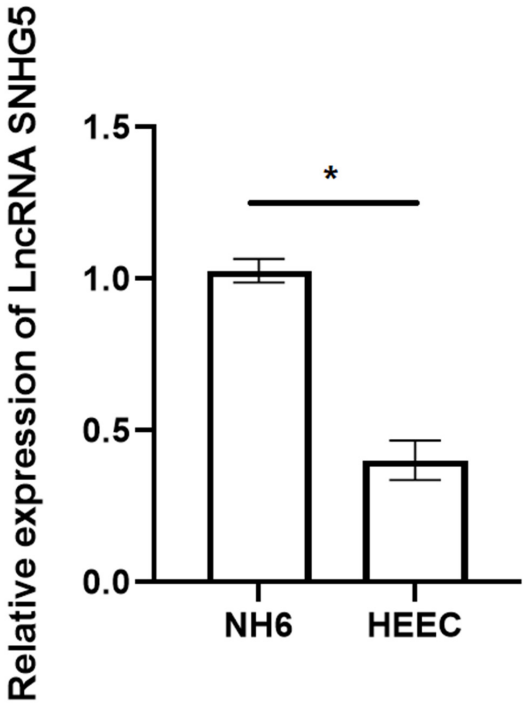

Figure 4. Comparison of LncRNA SNHG5 expression in HN6 and HEEC cells. **P<0.05.*

squamous carcinogenesis and disease progression.

Recent studies have shown that LncRNAs are involved in a variety of biological processes and are closely connected with multiple diseases. Since AFAP1-as1 [LncRNA produced from the antisense chain transcription of AFAP1 (actin fibrillin-associated protein 1) gene] was verified to be differentially expressed in esophageal adenocarcinoma, an increasing number of differentially expressed LncRNAs have been found in tumors [13, 14]. Previous studies have shown that LncRNA is differentially expressed in OPSCC and adjacent paracancerous tissues, and this abnormal expression of LncRNA may exert a considerable role in the tumorigenesis and progression of oropharyngeal carcinoma [15, 16]. LncRNA SNHG5, as a spliceosome of the host gene exon located at the U50 breakpoint of the chromatin genome, may be the crucial tumor-related gene [12]. Since the expression of LncRNA SNHG5 in both X-ray-irradiated TK6 cells and adjacent unirradiated cells has undergone remarkable changes, LncRNA SNHG5 may impose a vital role in

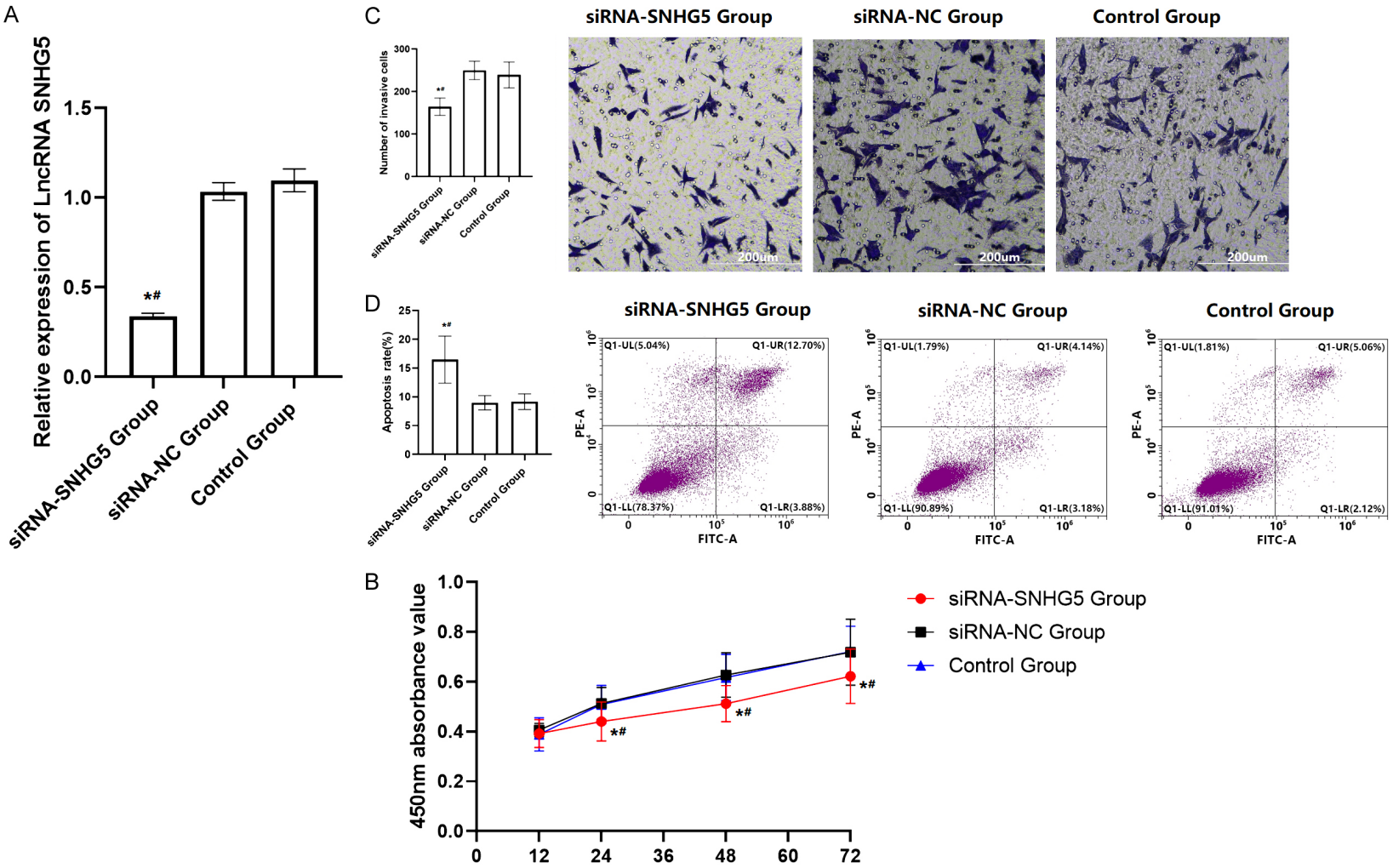

Figure 5. Effect of SNHG5 silencing on proliferation, invasion and apoptosis of the HN6 cells. A: Comparison of LncRNA SNHG5 expression in each group of cells after transfection. Compare with siRNA-NC Group, **P<0.05*; Compared with Control Group, *#P<0.05*. B: Comparison of cell proliferation in each group after transfection. Compared with siRNA-NC Group, **P<0.05*; Compared with siRNA-SNHG5 Group, *#P<0.05*. C: Comparison of invasion of cells in each group after transfection. Compared with siRNA-NC Group, **P<0.05*; Compared with Control Group, *#P<0.05*. D: Comparison of apoptosis in each group after transfection. Compared with siRNA-NC Group, **P<0.05*; Compared with Control Group, *#P<0.05*.

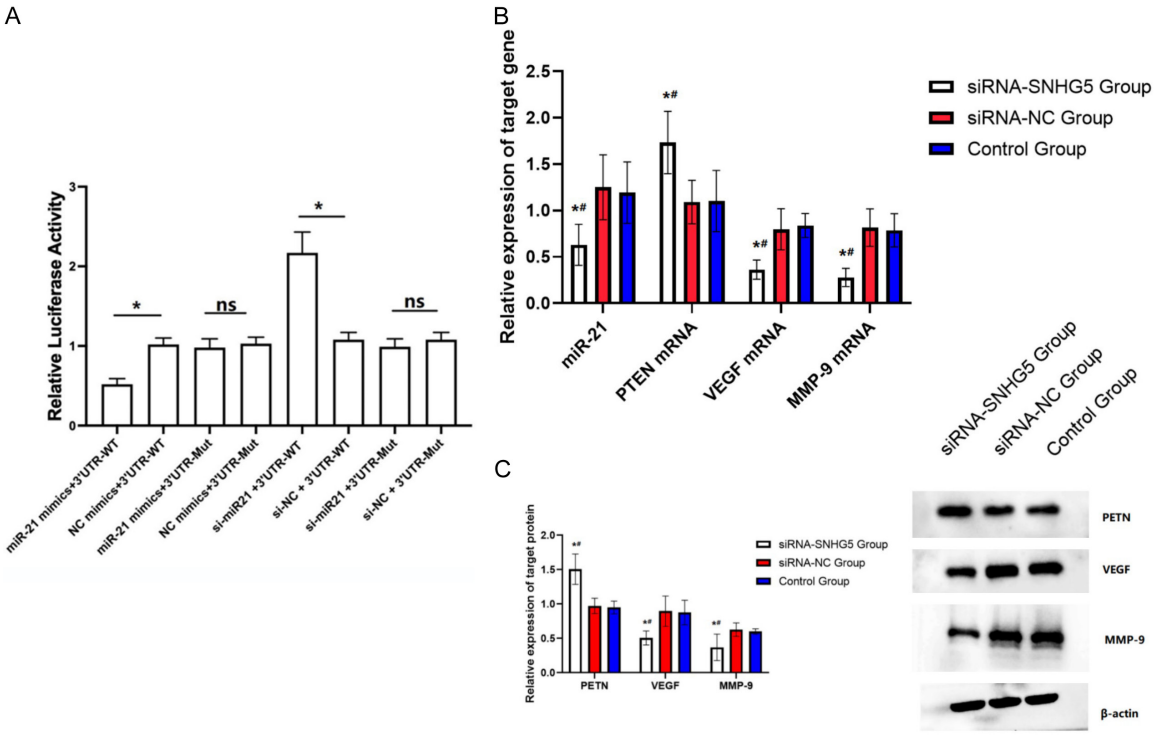

Figure 6. Effect of SNHG5 silencing on miR-21/PTEN signaling expression in HN6 cells. A: Luciferase reporter assay. *P<0.05, ns P>0.05. B. Comparison of miR-21, PTEN mRNA, VEGF mRNA and MMP-9 mRNA expression levels in transfected cells in HN6 cells. C: Comparison of protein expressions of PTEN, VEGF and MMP-9 in transfected cells of each group. Compared with siRNA-NC Group, **P<0.05*; Compared with Control Group, *#P<0.05.*

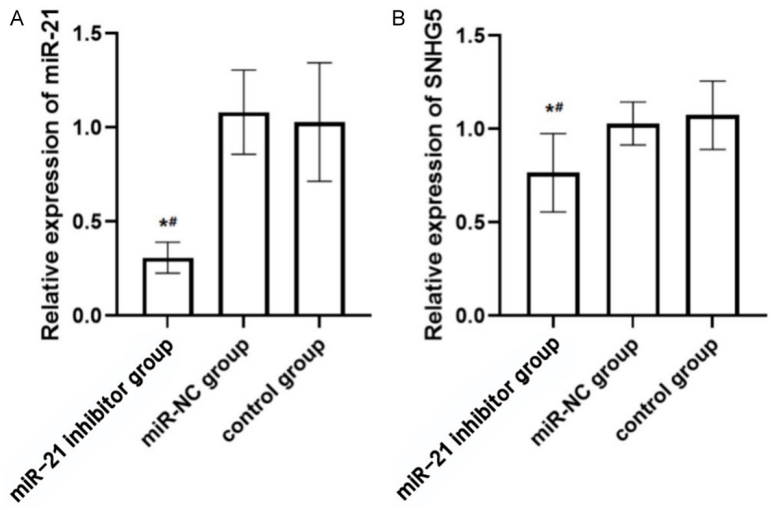

Figure 7. Effect of miR-21 inhibitor on SNHG5 expression in HN6 cells. A: The expression of miR-21 in each group of cells transfected with anti-miR-21. B: The influence of miR-21 interference on SNHG5 expression. Compared with miR-NC group, **P<0.05*; Compared with Control group, *#P<0.05*.

tumors [17-19]. In this study, the results of clinicopathological specimens showed that the relative expression of LncRNA SNHG5 in cancer tissues was obviously higher than that in adjacent paracancerous tissues. The expression of LncRNA SNHG5 in cancer tissues is related to TNM stage, lymph node metastasis and tumor differentiation of patients. Patients with low LncRNA SNHG5 expression had a significantly better survival than those with high LncRNA SNHG5 expression. The results, which are consistent with the studies reported by other scholars [20-22], revealed that there is abnormally high expression of LncRNA SNHG5 in ESCC patients, which is closely related to tumor malignancy and patient's survival prognosis. This may suggest that the abnormal expression of LncRNA SNHG5 may play a regulatory role in the occurrence and progression of OPSCC.

Furthermore, to investigate the regulatory role of LncRNA SNHG5 in OPSCC, we performed comprehensive in vitro analyses. Initial quantification revealed significantly elevated SNHG5 expression levels in human pharyngeal squamous cell carcinoma HN6 cells compared to immortalized oral epithelial HIOEC cells ($P<0.05$). Subsequent siRNA-mediated knockdown experiments demonstrated successful suppression of SNHG5 expression in treated groups (siRNA-SNHG5) relative to both negative control (siRNA-NC) and untreated control groups ($P<0.01$) [23, 24]. These cellular findings corroborated our clinical observations of SNHG5 overexpression in OPSCC specimens. To further characterize the functional consequences of SNHG5 downregulation, we systematically evaluated malignant phenotypes post-knockdown. The results collectively demonstrate that SNHG5 silencing effectively attenuates OPSCC progression by simultaneously inhibiting proliferation/migration while inducing apoptosis, findings consistent with emerging literature on oncogenic lncRNA functions [25, 26]. Notably, while our study establishes SNHG5's phenotypic impact, the precise molecular mechanisms mediating these effects remain to be elucidated.

The molecular mechanisms governing tumor cell proliferation and migration involve dysregulation of growth signaling, apoptotic pathways, motility regulators, and extracellular matrix remodeling processes [27-29]. PTEN is a tumor suppressor gene with dual-specific phosphohydrolase function that was discovered within recent years. It negatively regulates multiple intracellular signaling pathways and is closely related to the development of various malignant tumors such as lung cancer [19]. VEGF is an important pro-vascular growth factor, which can induce the formation of new blood vessels, thereby promoting the proliferation and migration of tumor cells [30]. MMP (especially MMP-9) has also been shown to exert key functions in migration and invasion of lung cancer cells [31, 32]. Notably, VEGF and MMP-9 expression levels correlate with tumor aggressiveness and are regulated downstream of PTEN [33]. Concurrently, miRNAs such as miR-21 - an oncogenic RNA overexpressed in multiple cancers - promote tumor progression by targeting PTEN and other tumor suppressors [34, 35]. Elevated miR-21 levels are clinically associated with advanced malignancy and poor prognosis. Building on these established pathways, our study investigated lncRNA SNHG5, previously reported as being upregulated in glioma [36]. We found that the expression of miR-21 was significantly reduced after the inhibition of lncRNA SNHG5 expression, and it was suggested that lncRNA SNHG5 could initiate tumor inhibition function by acting on miR-21. Therefore, we speculated that lncRNA SNHG5 might play a cancer-promoting role through miR-21. Then we further analyzed the effect of inhibiting LncRNA SNHG5 on the miR-21/PTEN signaling pathway. The results demonstrated that inhibiting the expression of LncRNA SNHG5 in HN6 cells may regulate the miR-21/PTEN signaling pathway, thereby inhibiting cell proliferation and migration, and promoting cell apoptosis. The miR-21/PTEN signaling pathway may be one of the mechanisms of LncRNA SNHG5 regulating the malignant biological behavior of tumor cells.

In summary, LncRNA SNHG5 is significantly upregulated in OPSCC tissues and cells. SNHG5 promotes tumor proliferation and invasion by regulating the miR-21/PTEN signaling axis and is strongly associated with poor patient prognosis, highlighting its potential as a therapeutic target. This current study is limited by a small sample size, and the mechanistic role of SNHG5 (e.g., its ceRNA regulatory mechanism) requires further validation through expanded cohorts, in vivo models, and interaction assays.

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Disclosure of conflict of interest

None.

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