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ORIGINAL RESEARCH

Influence of Human Papillomavirus E6 Gene Mutation on Brain-Derived Neurotrophic Factor Regulation and Cell Proliferation in Cervical Neoplasia: Insights Into Molecular Mechanisms

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Objective: To investigate the effects and mechanisms of human papillomavirus E6 (HPV16 E6) gene mutation on cervical cancer and cervical intraepithelial neoplasia grade I (CIN I) cell proliferation by regulating brain-derived neurotrophic factor (BDNF).

Methods: Real-time PCR was employed to measure mRNA levels of HPV16 E6 T350G, BDNF, and p53 in cervical cancer and CIN I tissues. Lentiviral vectors (pLV5-HPV16 E6 T350G and pLV5-vector) were constructed and transfected into human cervical epithelial cells. Real-time PCR validated successful infection and assessed mRNA changes induced by HPV16 E6 T350G. Western Blot was used to detect BDNF protein levels and PI3K/AKT phosphorylation. Cell proliferation was evaluated with the MTT assay, a standard method for assessing cell viability in vitro.

Results: Compared with CIN I cervical tissue, HPV16 E6 T350G and BDNF mRNA expression levels were positive in cervical cancer tissue, while p53 mRNA expression was negative; overexpression of HPV16 E6 T350G in human cervical epithelial cells upregulated BDNF mRNA and protein expression and activated its downstream signaling pathway PI3K/AKT, while reducing p53 protein expression; overexpression of HPV16 E6 T350G enhanced the proliferation ability of human cervical epithelial cells.

Conclusion: Overexpression of HPV16 E6 T350G can promote the proliferation ability of cervical cancer cells, possibly by upregulating BDNF expression to promote activation of the PI3K/AKT signaling pathway and decrease p53 expression.

Keywords: HPV16 E6, gene mutation, brain-derived neurotrophic factor, cervical cancer, cell proliferation

Introduction

Cervical cancer is one of the most common malignant tumors in the female reproductive system, with relatively high incidence and mortality rates globally.[1] Persistent infection with human papillomavirus (HPV), particularly high-risk subtypes such as HPV16, is a well-established primary etiological factor in cervical cancer development.[2] Multiple risk factors, including early sexual debut, multiple sexual partners, immunosuppression (eg, HIV infection), smoking, long-term use of oral contraceptives, and limited access to cervical cancer screening programs, contribute to HPV acquisition and persistence, thereby increasing the likelihood of malignant transformation.[3] In 2019, HPV infection was attributed to approximately 620,000 new cancer cases in women and 70,000 cases in men worldwide.[4] By 2022, cervical cancer ranked as the fourth most prevalent cancer among women, with approximately 660,000 new cases and around 350,000 deaths globally.[5] Cervical cancers account for over 90% of HPV-related cancers in women.[6] Despite significant advancements in cervical cytology screening and HPV vaccination programs, cervical cancer remains a major health concern, particularly in resource-limited settings.[7]

During HPV infection, the viral oncoproteins E6 and E7 play critical roles in cellular transformation by disrupting key regulatory pathways, including cell cycle control, apoptosis, and DNA repair.[8,9] These disruptions enable the virus to evade host defenses and promote the malignant transformation of cervical epithelial cells. Among these, the HPV16 E6

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oncoprotein is of particular interest due to its role in degrading tumor suppressor proteins such as p53, thus contributing to oncogenesis.[10]

Recent studies have identified specific mutations within the HPV16 E6 gene that may influence its oncogenic potential. One such mutation, the T350G single nucleotide polymorphism, results in an amino acid substitution in the E6 protein and has been found to occur frequently in cervical cancer tissues.[11] This mutation may alter the interaction of the E6 protein with its cellular targets, potentially affecting processes such as cell proliferation, apoptosis, and transformation.[12] However, the clinical implications of this mutation remain unclear. Understanding the functional consequences of the HPV16 E6 T350G mutation is critical, as it may provide insights into mechanisms of cancer progression and identify potential biomarkers or therapeutic targets. The selection of this mutation for study is based on its reported prevalence in cervical cancer tissues and its suspected role in altering E6 protein function, highlighting its potential as a key driver in cervical carcinogenesis.

Additionally, neurotrophic factors in the tumor microenvironment, such as brain-derived neurotrophic factor (BDNF), are gaining attention for their roles in tumorigenesis.[13,14] BDNF, known for its functions in neuronal survival and differentiation, has been implicated in the proliferation and progression of various cancers, including cervical cancer.[15,16] BDNF can activate multiple signaling pathways, such as the PI3K/AKT pathway, which in turn modulates downstream molecules like p53. Inactivation of p53 via this pathway is a common mechanism by which cancer cells evade apoptosis and enhance proliferative capacity.[17,18] However, the relationship between HPV16 E6 T350G and BDNF expression, and their combined effects on cervical cancer development, remains unexplored.

Cervical intraepithelial neoplasia grade I (CIN I) represents an early abnormality often considered a precursor lesion to cervical cancer. Comparative analysis of molecular and cellular differences between CIN I and cervical cancer tissues can provide valuable insights into the progression from benign lesions to malignancy.[19] Therefore, this study focuses on the role of the HPV16 E6 T350G mutation in regulating BDNF expression and its subsequent impact on cell proliferation in cervical cancer and CIN I. By elucidating these mechanisms, we aim to uncover new pathways involved in HPV-mediated carcinogenesis and provide novel targets for the prevention, diagnosis, and treatment of cervical cancer.

Materials and Methods

Main Materials

Human cervical epithelial cells (obtained from Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences), LV5-HPV 16 L83V (T350G) overexpression lentivirus (Shengwu Biotechnology Co., Ltd)., AKT antibody, p-AKT antibody, p-PI3K antibody, PI3K antibody, TrKB antibody, BDNF antibody, goat anti-rabbit IgG, internal reference antibody GAPDH, internal reference antibody β-actin (Abcam), ECL luminescence solution (7 Sea biotech), TRI-pure total RNA extraction reagent (Bai Tek), Super M-MLV reverse transcriptase (Bai Tek), microplate reader (ELX-800, BIOTEK), fluorescence quantitative PCR instrument (Exicycler 96, BIONEER), MTT cell proliferation and cytotoxicity detection kit (Beyotime), −70°C ultra-low temperature freezer (Dw HL-668), primers synthesized by Kingsray Biotechnology Co., Ltd.

Tissue Specimens

Ten cases of cervical squamous cell carcinoma IA1-IB2 after radical hysterectomy and ten cases of cervical tissue excised due to CIN I were collected, with ages ranging from 33 to 61 years old, and an average age of (51.68±4.17) years old. None of the patients had received radiotherapy or chemotherapy before surgery. The specimens were diagnosed by three pathologists from our hospital, and all patients were informed and consented to participate in this study by signing relevant documents. This study was approved by the Hebei Zhongshihuo Central Hospital Ethics Committee, with an approval number of EXK024527145. This study complies with the Declaration of Helsinki. After collection, the specimens were stored in a −80°C freezer.

Inclusion Criteria

1) Patients diagnosed with IA1-IB2 after radical hysterectomy or cervical tissue excised due to CIN I.
2) Age between 33 to 61 years old.
3) No history of radiotherapy or chemotherapy prior to surgery.
4) Specimens diagnosed by three pathologists from the hospital to ensure accurate classification.
5) Patients who provided informed consent to participate in the study by signing relevant documents.
6) Availability of specimens stored in a −80°C freezer for further analysis.

Exclusion Criteria

1) Patients diagnosed with cervical cancer other than squamous cell carcinoma or with pre-cancerous lesions other than CIN I.
2) History of previous treatment for cervical cancer or pre-cancerous lesions.
3) Concurrent medical conditions or treatments that could affect the study outcomes or interpretation of results.
4) Specimens deemed inadequate for analysis due to poor quality or insufficient tissue sampling.
5) Patients who did not provide informed consent to participate in the study.
6) Specimens not stored properly or unavailable for analysis.

Cell Culture and Infection

Human cervical epithelial cells were cultured in DMEM medium containing 10% fetal bovine serum at 37°C in a 5% CO2 incubator.

To construct the HPV16 E6 T350G lentiviral overexpression vector (pLV5-HPV16 E6 T350G), the HPV16 E6 gene containing the T350G mutation was amplified by PCR and inserted into the pLV5 vector. The vector was verified by Sanger sequencing to ensure the presence of the T350G mutation. The sequencing primers are listed in Table 1.

Steps for vector construction and sequence verification: (1) DNA from pLV5-HPV16 E6 T350G was extracted using a plasmid mini kit. (2) PCR was performed to amplify the E6 region, followed by Sanger sequencing. (3) Sequencing results were analyzed to confirm the T350G mutation at the specific site.

Once the lentiviral vector was constructed, HPV16 E6 T350G lentiviral overexpression vector (pLV5-HPV16 E6 T350G) and control vector (pLV5-vector) were transfected into human cervical epithelial cells at the logarithmic growth phase. Non-transfected human cervical epithelial cells were used as an additional control.

Real-Time PCR

1) Sample preparation: Fifty milligrams of cervical tissue from both cervical cancer and CIN I samples were weighed and frozen in liquid nitrogen to preserve RNA integrity. The frozen tissue samples were then ground to a fine powder to facilitate RNA extraction.

2) RNA extraction: Total RNA was extracted from the ground tissue samples using a total RNA extraction reagent. This step involves lysing the cells to release RNA and then isolating the RNA from other cellular components such as proteins and lipids. The extracted RNA contains a mixture of RNA molecules, including messenger RNA (mRNA), ribosomal RNA (rRNA), and transfer RNA (tRNA).

Table 1 Primer Sequences

–	–	Primer Sequences
β-actin	F	5′- GGAAATCGTGCGTGACATC AA - 3′
	R	CCAAGAAGGAAGGCTGGAAAA
HPV16 E6 T350G	F	5′- TATAAAACTAAGGGCGTAAC - 3′
	R	5′- CATGCAATGTAGGT GTATCT - 3′
BDNF	F	5′- TGCGGGAGGAATTTCTGAGT - 3′
	R	5′- CTTAA AGCACGAGGTCC - 3′
P53	F	5′- TGCGTGTGGAGTATTTGATG - 3′
	R	5′- 5TGGTACAGTCAGAGCCAACCTC - 3′

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3) cDNA synthesis: The extracted RNA was reverse transcribed into complementary DNA (cDNA) using a cDNA synthesis reagent. Reverse transcription is a process where the enzyme reverse transcriptase synthesizes a single-stranded cDNA molecule using the RNA template. This step converts the RNA, including the target mRNA (ECRG4 mRNA in this case), into cDNA, which is more stable and amplifiable.

Primer design: Specific primer sequences targeting the ECRG4 gene were designed for use in the real-time PCR reaction. The primer sequences are listed in Table 1.

4) Real-time PCR setup: The cDNA samples were then subjected to real-time PCR using a fluorescence quantitative instrument, such as the ExicyclerTM 96 fluorescence quantitative instrument. Real-time PCR involves the amplification of the target DNA sequence in the presence of fluorescent reporter molecules that emit fluorescence upon binding to the amplified DNA. The fluorescence intensity is measured at each cycle of amplification, allowing for the quantification of the initial amount of target DNA.

5) Quantitative analysis: The fluorescence signals obtained during the real-time PCR reaction were analyzed using the 2-ΔΔCt method.

Western Blot

Protein was extracted from each cell group for standard curve plotting. Fifteen to thirty micrograms of protein were subjected to SDS-PAGE electrophoresis. After transferring to a PVDF membrane and blocking, different primary antibodies (including rabbit anti-BDNF, p-PI3K, PI3K, p-AKT, AKT, diluted at 1:500) were added and incubated overnight at 4°C. Subsequently, the membrane was washed with TBST, followed by the addition of secondary antibodies (goat anti-rabbit IgG-HRP, diluted at 1:10,000), and incubated at 37°C for 40 minutes. Finally, the membrane was incubated with ECL luminescence solution, allowed to stand for 5 minutes, and then exposed and developed in a darkroom. The grayscale values of the target bands on the film were scanned and collected for analysis of optical density.

MTT Cell Proliferation

After cell infection, 20 μL of MTT at a concentration of 0.2 mg/mL was added to each well of a 96-well plate, with 3 replicate wells and blank wells set for each group. The cells were then cultured for 4–6 hours, the supernatant was discarded, and 150 μL of DMSO was added to each well. The plate was shaken on a horizontal shaker until the formazan crystals were completely dissolved. The absorbance was then measured at a wavelength of 570 nm, and the formula for calculating cell viability was: (Experimental group OD value / Control group OD value) × 100%.

Statistical Analysis

SPSS 20.0 software was used for data analysis. Descriptive statistics for continuous data were presented as ($\bar{x} \pm s$), and between-group comparisons were analyzed using independent sample t-tests. P- values were calculated using Fisher's Exact Test (FET) for categorical data with expected frequencies less than 5. A P value <0.05 indicated statistical significance.

Results

Baseline Characteristics of Cervical Tissue Samples

There were no statistically significant differences in baseline characteristics between patients with cervical invasive cancer (IA1-IB2) undergoing radical hysterectomy and those with CIN I undergoing LEEP (P > 0.05), indicating comparability (Table 2).

mRNA Expression of Various Genes in Cervical Intraepithelial Neoplasia (CIN I) and Cervical Cancer Tissues

In comparing the gene expression levels between CIN I cervical tissue and cervical cancer tissue, significant differences were observed. Specifically, the mRNA expression of HPV16 E6 T350G was markedly elevated in cervical

Table 2 Baseline Characteristics of Cervical Tissue Samples

	ICC Group (n=10)	CIN I Group (n=10)	t/FET	p
Age	52.25±4.54	49.72±4.36	0.597	0.284
BMI (kg/m²)	22.33±2.41	22.16±2.47	0.484	0.340
Parity	2.17±0.57	2.08±0.55	0.938	0.337
Comorbidities			0.297	0.565
Hypertension	3(30.00%)	2(20.00%)		
Diabetes	2(20.00%)	1(10.00%)		
History of uterine procedures	3(30.00%)	2(20.00%)	0.651	0.139
Family history of cervical cancer	2(20.00%)	2(20.00%)	0.738	0.552

Abbreviations: ICC Group, Cervical invasive cancer group (IA1-IB2 stages after radical hysterectomy); CIN I Group, Cervical intraepithelial neoplasia grade I group (after LEEP resection).

cancer tissue (6.59±0.11) compared to CIN I cervical tissue (0.91±0.04). Similarly, the expression of brain-derived neurotrophic factor (BDNF) exhibited a substantial increase in cervical cancer tissue (10.67±0.65) compared to CIN I cervical tissue (1.04±0.02). Conversely, the expression of tumor protein 53 (p53) showed a notable decrease in cervical cancer tissue (0.23±0.03) compared to CIN I cervical tissue (0.95±0.02). These findings suggest a potential association between these gene expression alterations and the progression from CIN I to cervical cancer ($P<0.05$), as shown in Figure 1.

To confirm the successful transfection of HPV16 E6 T350G, Western blot analysis was performed to evaluate protein expression levels. The results demonstrated a significant upregulation of HPV16 E6 T350G protein in the pLV5-HPV16 E6 T350G group compared to the pLV5-vector group, with relative expression levels of 3.45 ± 0.12 vs 1.00 ± 0.05 ($P < 0.05$, Figure 2).

Influence of HPV16 E6 T350G on BDNF Expression in Human Cervical Epithelial Cells

The investigation of BDNF expression in response to HPV16 E6 T350G overexpression was motivated by the potential regulatory relationship between these two factors in cervical cancer progression. By analyzing BDNF expression levels following HPV16 E6 T350G infection, we aimed to elucidate the molecular mechanisms underlying the interaction between HPV infection and BDNF signaling in cervical cancer. Real-time PCR and Western Blot results showed a significant enhancement in BDNF mRNA and protein expression levels following the upregulation of HPV16 E6

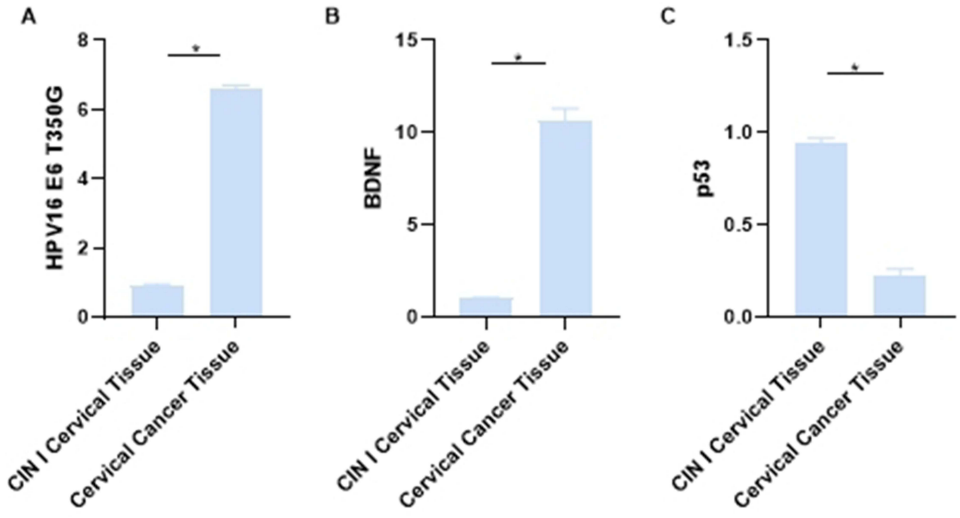

Figure 1 mRNA Expression of Various Genes in Cervical Intraepithelial Neoplasia (CIN I) and Cervical Cancer Tissues; (**A**) HPV16 E6 T350G, (**B**) BDNF, (**C**) p53. *P < 0.05.

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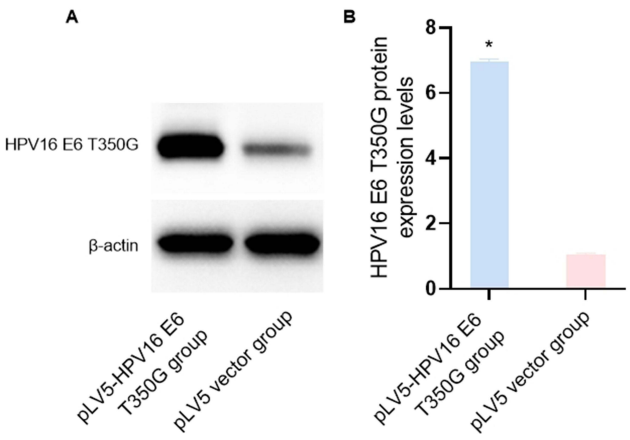

Figure 2 Validation of HPV16 E6 T350G expression in human cervical epithelial cells. (**A**) Western blot analysis of HPV16 E6 T350G protein levels in the pLV5-HPV16 E6 T350G group compared to the pLV5-vector group. β-actin was used as a loading control. (**B**) Quantitative analysis of HPV16 E6 T350G protein expression levels. Data are expressed as the mean ± SD. *P < 0.05 versus pLV5-vector.

T350G expression in human cervical epithelial cells (P < 0.05), suggesting that BDNF may serve as a downstream regulatory molecule of HPV16 E6 T350G variation in cervical cancer, as shown in Table 3.

Influence of HPV16 E6 T350G on the PI3K/Akt Signaling Pathway and p53 Expression in Human Cervical Epithelial Cells

The investigation into the PI3K/Akt signaling pathway and p53 expression aimed to unravel the downstream effects of HPV16 E6 T350G overexpression on cellular signaling and tumor suppressor pathways. Dysregulation of the PI3K/Akt pathway and p53 expression has been implicated in cervical cancer progression, suggesting their potential involvement in HPV-mediated carcinogenesis. By assessing the phosphorylation levels of PI3K and Akt and quantifying p53 expression levels following HPV16 E6 T350G infection, we sought to elucidate the molecular mechanisms underlying the oncogenic properties of this viral mutation. Western Blot results revealed an upregulation of phosphorylated levels of PI3K and Akt in human cervical epithelial cells expressing HPV16 E6 T350G (P < 0.05), indicating potential activation of the PI3K/Akt signaling pathway by HPV16 E6 T350G via BDNF. Additionally, Real-time PCR experimental results demonstrated a significant decrease in p53 expression levels upon upregulation of HPV16 E6 T350G (P < 0.05), as shown in Table 4.

Table 3 Influence of HPV16 E6 T350G on BDNF Expression in Human Cervical Epithelial Cells (n=3, $\bar{x} \pm s$)

BDNF	Control	pLV5-vector	pLV5-HPV16 E6 T350G
mRNA	0.96±0.02*	0.98±0.03*	6.91±0.08
Protein	1.02±0.06*	1.05±0.07*	8.14±0.09

Note: Compared to the pLV5-HPV16 E6 T350G group, *P < 0.05.

Table 4 Influence of HPV16 E6 T350G on the PI3K/Akt Signaling Pathway and p53 Expression in Human Cervical Epithelial Cells (n=3, $\bar{x} \pm s$)

Protein	Control	pLV5-vector	pLV5-HPV16 E6 T350G
pPI3K/PI3K	0.94±0.11*	1.03±0.04*	6.47±0.09
pAkt/Akt	0.96±0.04*	0.91±0.03*	5.72±0.08
mRNA p53	0.98±0.05*	0.94±0.02*	0.26±0.03

Note: Compared to the pLV5-HPV16 E6 T350G group, *P < 0.05.

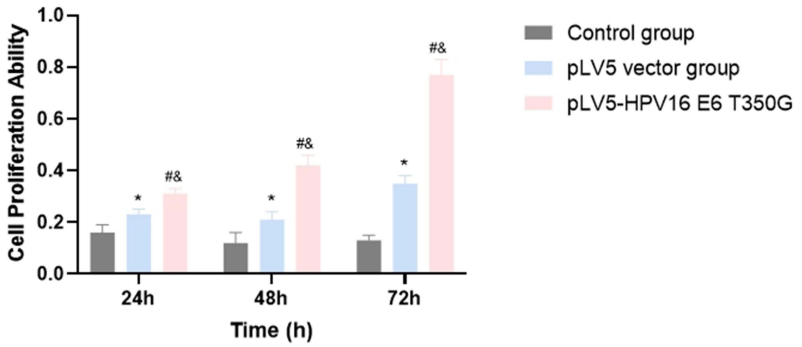

Figure 3 Effect of HPV16 E6 T350G Overexpression on the Proliferative Ability of Human Cervical Epithelial Cells at Different Time Points. Statistical significance was indicated by the following symbols: *P < 0.05, comparing pLV5-vector to Control at the same time point; #P < 0.01, comparing pLV5-HPV16 E6 T350G to Control at the same time point; and P < 0.01, comparing pLV5-HPV16 E6 T350G to pLV5-vector at the same time point.

MTT Assay Results Showing Enhanced Proliferative Ability of Human Cervical Epithelial Cells with HPV16 E6 T350G Overexpression

At all time points (24 h, 48 h, and 72 h), the overexpression of HPV16 E6 T350G significantly enhanced the proliferative ability of human cervical epithelial cells compared to both the Control and pLV5-vector groups. Specifically, at 24 h, the optical density (OD) value of the pLV5-HPV16 E6 T350G group (0.31±0.02) was significantly higher than that of the Control group (0.16±0.03, P < 0.01) and the pLV5-vector group (0.23±0.02, and P < 0.01), with the pLV5-vector group also showing a modest increase compared to the Control group (P < 0.05). At 48 h, the OD value of the pLV5-HPV16 E6 T350G group (0.42±0.04) demonstrated a marked increase compared to the Control (0.12±0.04, #P < 0.01) and pLV5-vector groups (0.21±0.03, and P < 0.01), while the pLV5-vector group significantly exceeded the Control group (P < 0.05). At 72 h, the pLV5-HPV16 E6 T350G group displayed the highest OD value (0.77±0.06), significantly surpassing both the Control (0.13±0.02, #P < 0.01) and pLV5-vector groups (0.35±0.03, and P < 0.01), with the pLV5-vector group also showing a significant increase compared to the Control group (P < 0.05). These results suggest a time-dependent enhancement of cell proliferation by HPV16 E6 T350G overexpression, as shown in Figure 3.

Discussion

The findings of this study demonstrated that the expression level of HPV16 E6 T350G in cervical cancer tissues was significantly higher compared to CIN I tissues, corroborating prior research.[20] This upregulation was accompanied by an increase in BDNF expression, suggesting that HPV16 E6 T350G may promote cervical cancer development through the regulation of BDNF. Subsequent in vitro experiments confirmed that overexpression of HPV16 E6 T350G in cervical epithelial cells led to elevated mRNA and protein levels of BDNF, aligning with previous studies.[21] Furthermore, the activation of the PI3K/AKT signaling pathway was observed, as evidenced by increased phosphorylation of PI3K and AKT, indicating that HPV16 E6 T350G may contribute to cervical carcinogenesis through this pathway. This finding is consistent with earlier reports highlighting the role of PI3K/AKT in cancer progression.[22]

Importantly, the study also found that HPV16 E6 T350G overexpression resulted in p53 downregulation and enhanced cellular proliferation. These observations align with existing literature reporting p53 inactivation in cervical epithelial cells in various populations, such as Indonesian women with cervical cancer.[23] Collectively, these results provide new insights into the mechanisms by which HPV16 E6 T350G promotes cervical cancer development, particularly through the interplay of BDNF upregulation, PI3K/AKT pathway activation, and p53 downregulation.

The results underscore the oncogenic potential of the HPV16 E6 T350G mutation and highlight its relevance as a potential therapeutic target. The upregulation of BDNF and the activation of the PI3K/AKT signaling pathway suggest specific molecular targets for intervention. Targeted therapies designed to inhibit BDNF expression or disrupt the PI3K/AKT signaling cascade could provide new avenues for treating cervical cancer. Furthermore, the observed downregulation of p53 underscores the importance of restoring p53 activity as a therapeutic strategy, which could be explored through the development of small molecule inhibitors or gene therapy approaches.

In the broader clinical context, the findings highlight the need for the integration of HPV genetic profiling into cervical cancer management. Screening for HPV16 E6 T350G mutations in clinical settings could enable risk stratification and facilitate personalized treatment strategies. For instance, patients identified as carriers of this mutation could benefit from targeted therapies or closer monitoring for disease progression. Additionally, these findings could inform vaccine design by identifying critical regions of the E6 protein for immunogenic targeting, potentially improving the efficacy of existing HPV vaccines.

Study Limitations and Future Directions

While this study provides valuable mechanistic insights, several limitations should be addressed in future research. First, the experiments were conducted in vitro, which may not fully capture the complexity of in vivo tumor development. Animal models or patient-derived xenografts could be used to validate these findings and explore the tumor microenvironment's role. Second, this study focused on the HPV16 E6 T350G mutation in isolation, neglecting potential interactions with other HPV genes, such as E7, or host genetic variations. Further studies could investigate the combined effects of E6 and E7 mutations on cervical carcinogenesis. Third, while the study explored the PI3K/AKT pathway, additional downstream targets of BDNF or alternative signaling pathways may contribute to the observed effects. Investigating these pathways could provide a more comprehensive understanding of the mutation's role in cervical cancer. Lastly, the lack of clinical data limits the study's translational potential. Larger cohort studies with clinical samples are needed to validate the findings and assess their relevance in diverse populations.

Broader Impact

This study contributes to the growing body of evidence linking HPV genetic variations to cervical cancer progression. By elucidating the molecular mechanisms underlying HPV16 E6 T350G's effects, it provides a foundation for the development of novel diagnostic and therapeutic strategies. The identification of actionable molecular targets, such as BDNF and the PI3K/AKT pathway, highlights the potential for translating these findings into clinical practice. Moreover, the results emphasize the importance of a multidisciplinary approach to cervical cancer research, integrating molecular biology, clinical oncology, and public health to address the global burden of this disease.

Conclusion

The study demonstrates that the HPV16 E6 T350G mutation plays a pivotal role in the progression of cervical cancer by modulating key molecular pathways. Specifically, this mutation significantly enhances BDNF expression, activates the PI3K/AKT signaling pathway, and suppresses p53 expression, collectively promoting increased proliferative capacity in cervical epithelial cells. These findings suggest that HPV16 E6 T350G may serve as a critical biomarker for cervical cancer risk assessment and a potential therapeutic target. Further research into the molecular mechanisms of this mutation could provide new avenues for the prevention, diagnosis, and treatment of cervical cancer.

Disclosure

The authors report no conflicts of interest in this work.

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