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Original Research

Tripartite Motif-Containing 1 Influences the Prognosis of Cervical Cancer

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Abstract

Background: Deoxyribonucleic acid (DNA) damage repair pathways synergistically promote cervical carcinogenesis. The role of tripartite motif-containing 11 (TRIM11) in DNA repair may influence genomic stability in cervical cancer (CC) and modulate treatment response. This study aimed to analyze the expression and prognostic significance of TRIM11 in CC and across multiple cancer types (pan-cancer analysis). **Methods**: TRIM11 expression patterns in CC were investigated through integrated bioinformatics analyses using two independent cohorts: transcriptomic data from The Cancer Genome Atlas (TCGA) and the Gene Expression Omnibus (GEO) dataset GSE67522. Experimental validation of TRIM11 overexpression in clinical CC specimens was performed through molecular techniques, including quantitative PCR and Western blotting. Survival outcomes were assessed using Kaplan-Meier method, revealing significant correlations between TRIM11 expression levels and both progression-free survival (PFS) and overall survival (OS) rates in TCGA CC cases. Functional pathway associations were elucidated through gene set enrichment analysis (GSEA), identifying TRIM11-related oncogenic mechanisms. Furthermore, a comprehensive pan-cancer evaluation employing TCGA multi-omics data systematically characterized the prognostic relevance of TRIM11 across diverse malignancies. **Results**: TCGA cohort analysis demonstrated a statistically significant elevation in TRIM11 expression levels in tumor tissues compared to normal controls ($p < 0.0001$), with consistent validation observed in the GSE67522 cohort ($p < 0.0001$). Molecular validation experiments confirmed concurrent upregulation of TRIM11 at both the transcriptional (quantitative reverse transcriptase PCR (qRT-PCR), $p < 0.05$) and proteomic (Western blot, $p < 0.05$) levels in CC tissues compared to paired adjacent normal samples. Notably, within the context of human papillomavirus (HPV) infection, the GSE67522 dataset highlighted the pivotal role of TRIM11 during malignant transformation, show a significant difference in expression between HPV-positive cancer tissues and matched normal cervical epithelia ($p < 0.001$). In the TCGA dataset, OS ($p = 0.007$; HR [high-expression group] = 1.899; 95% confidence interval [CI], 1.189–3.033) and PFS ($p = 0.003$; HR = 2.035; 95% CI, 1.266–3.273) were significantly longer in patients with CC with lower TRIM11 expression compared to those with higher TRIM11 expression. Subsequently, GSEA in the TCGA dataset showed that TRIM11 is involved in the transforming growth factor beta (TGF-β), calcium, wingless/integrated (WNT), and mitogen-activated protein kinase (MAPK) pathways in CC ($p < 0.0001$). Pan-cancer analysis showed that TRIM11 expression differed significantly between various tumor tissues and their corresponding normal tissues, and was closely associated with prognosis across several cancer types. **Conclusions**: This study demonstrated that TRIM11 is overexpressed in CC, and that its overexpression is associated with poor prognosis. Furthermore, its expression was significantly correlated with prognosis across multiple cancers.

Keywords: tripartite motif-containing 11; prognosis; cervical cancer; pan-cancer

1. Introduction

Cervical cancer (CC) remains a major global health burden, ranking as the fourth most prevalent malignancy among women. Recent estimates indicate over 600,000 new diagnoses and 340,000 fatalities in 2024, with disproportionate impacts on resource-limited regions [1]. Histologically, squamous cell carcinoma dominates (80% of cases), contrasting with adenocarcinomas (15–20%), which exhibit divergent molecular pathogenesis [2,3]. In China alone, 2021 recorded 132,788 incident cases and 49,841 deaths, underscoring its persistent public health challenge [4]. Key risk factors encompass early sexual debut, multiparity, tobacco use, prolonged oral contraceptive intake, and persistent human papillomavirus (HPV) infection [5,6]. Prognosis starkly correlates with staging: early lesions demonstrate 73–98% 5-year survival, plummeting to <20% in advanced disease [7,8]. Delayed detection, often linked to irregular screening, exacerbates recurrence risks and mortality [9], emphasizing the imperative for robust early diagnostic protocols.

Tripartite motif-containing 11 (TRIM11), an E3 ubiquitin ligase within the TRIM family, orchestrates ubiquitin-mediated protein turnover and immune modulation [10]. Beyond its canonical role in cellular homeostasis, this mul-

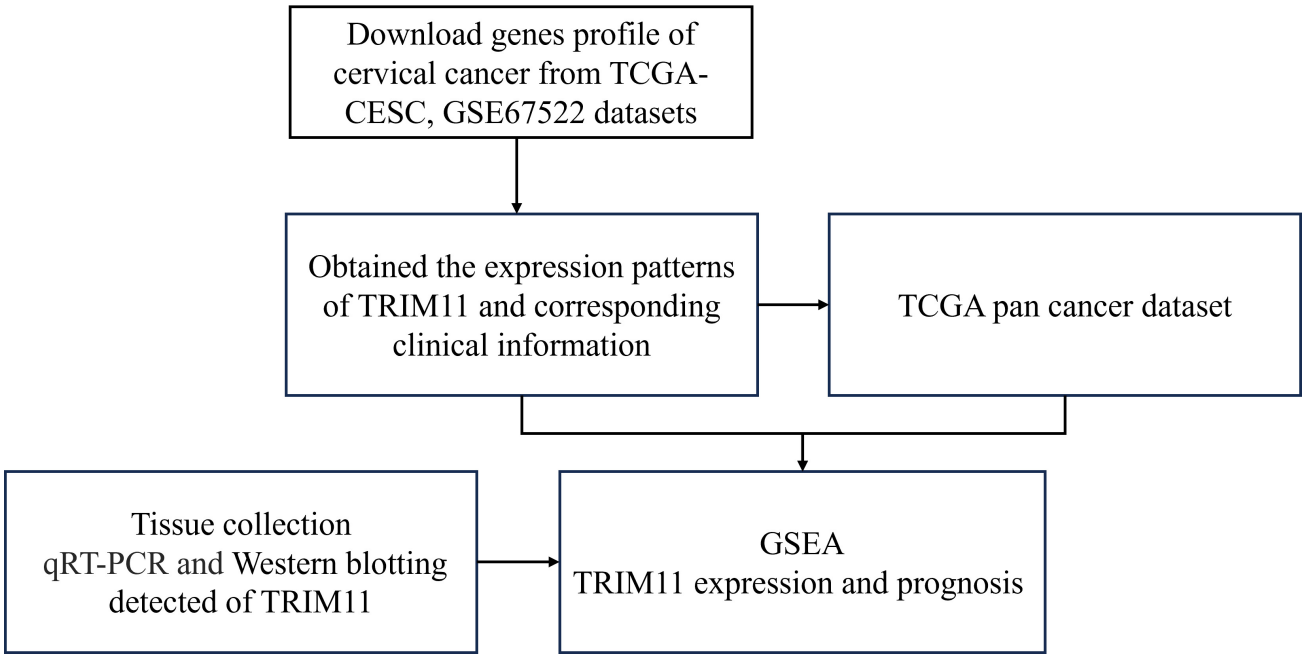

Fig. 1. Workflow of the study. TCGA, The Cancer Genome Atlas; TRIM11, Tripartite motif-containing 11; GSEA, Gene set enrichment analysis; qRT-PCR, quantitative reverse transcriptase PCR; CESC, cervical squamous cell carcinoma.

tifunctional protein intersects with oncogenesis, genetic disorders, and viral pathogenesis [11–13]. Emerging evidence implicates TRIM11 in tumor progression through post-translational regulation of critical signaling pathways, positioning it as a potential therapeutic target [10]. Dysregulated TRIM11 activates related signaling pathways, thus affecting the phenotype of tumor cells, and is closely associated with tumor development [14]. In lung cancer, TRIM11 expression is associated with tumor size, tumor node metastasis (TNM) stage, lymph node metastasis, and overall survival (OS) [15]. Therefore, we speculate that TRIM11 is a key gene contributing to tumor development in lung cancer. However, the role of TRIM11 in CC remains unclear.

In this study, we analyzed the expression and prognostic value of TRIM11 in CC and various other cancer types.

2. Materials and Methods

2.1 Data Collection and Workflow

TRIM11 expression data and associated clinical information were retrieved from two publicly available databases: The Cancer Genome Atlas (TCGA, https://www.cancer.gov/ccg/research/genome-sequencing/tcga) and the GSE67522 dataset (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE67522), which provided comprehensive genomic and clinical profiles of cervical cancer patients. TRIM11 protein expressions and mRNA levels were derived from 4 cancer and 4 normal fresh tissues. The workflow is illustrated in Fig. 1.

2.2 Analysis of TRIM11 Expression Pattern

The R package clusterProfiler (https://bioconductor.org/packages/clusterProfiler/) was used to analyze the expression of TRIM11 in CC in The Cancer Genome Atlas-Cervical Squamous Cell Carcinoma (TCGA-CESC) and GSE67522 datasets. The samples in both datasets were divided into high- and low-expression groups based on the median expression level of TRIM11. The survival status of the patients was obtained from the datasets. Subsequently, the prognostic value of TRIM11 in CC was validated in the TCGA-CESC dataset.

2.3 Gene Set Enrichment Analysis

Gene set enrichment analysis (GSEA) was conducted using version 3.0 of the software suite (Broad Institute, Inc., Cambridge, MA, USA, accessible at http://software.broadinstitute.org/gsea). Samples were stratified into high- and low-expression cohorts using the median TRIM11 expression level as the threshold ($\geq$50% vs. $<$50%). Pathway enrichment analysis utilized the c2.cp.kegg.v7.4.symbols.gmt subset from the Molecular Signatures Database (https://www.gsea-msigdb.org). Gene sets were filtered by size constraints (5–5000 genes per set), and significance testing incorporated 1000 permutations for robust statistical validation. Pathway associations were deemed significant if meeting either of the following criteria: nominal $p < 0.05$ or false discovery rate (FDR) $<$0.25.

2.4 Tissue Collection

Four cervical cancer and four normal fresh tissues were collected and stored at –80 °C until subsequent quan-

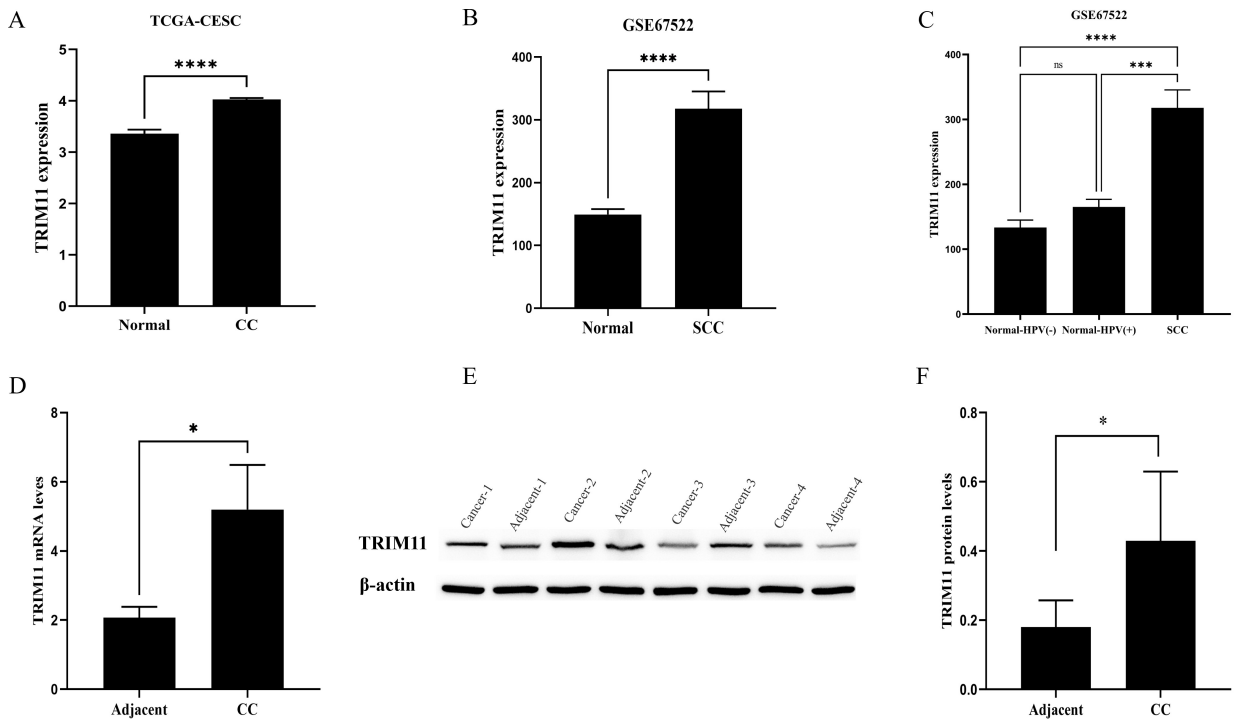

Fig. 2. Expression of TRIM11 in cervical cancer (CC). (A,B) TRIM11 was overexpressed in CC tissues in the TCGA-CESC and GSE67522 datasets. (C) TRIM11 expression in human papillomavirus (HPV)-positive CC and normal cervical tissues. (D–F) mRNA and protein expression levels of TRIM11 in CC and adjacent normal tissues. *, $p < 0.05$; ***, $p < 0.001$; ****, $p < 0.0001$; ns, $p > 0.05$.

titative reverse transcription PCR (qRT-PCR) and Western blotting analysis. All tissues were collected at Zhuzhou Central Hospital, Zhuzhou, Hunan, China, between June and July 2024. The protocol for tissue harvest was approved by the Ethics Committee of Zhuzhou Central Hospital (No. 20231046), and informed consent was obtained per Declaration of Helsinki guidelines from each eligible participant.

2.5 Quantitative Reverse Transcription Polymerase Chain Reaction and Western Blotting

2.5.1 qRT-PCR

Total RNA was isolated using Trizol reagent (Invitrogen, Cat. #15596026, Waltham, MA, USA) with homogenization via a KZ-III-FP homogenizer (Servicebio, Wuhan, Hubei, China). Reverse transcription employed the PrimeScript RT Master Mix (Takara, Cat. #RR036A, Dalian, Liaoning, China), followed by quantitative PCR (qPCR) amplification on a QuantStudio 5 System (Thermo Fisher, Waltham, MA, USA) with β-actin normalization (primers validated via NCBI Primer-BLAST: https://www.ncbi.nlm.nih.gov/tools/primer-blast/index.cgi, Table 1). The $2^{-\Delta\Delta CT}$ method was used to calculate the fold change in TRIM11 expression between the cancer and normal groups.

Table 1. RT-PCR primer information.

Gene name	Primer sequence (5′–3′)
H-β-actin-F	GAGCACAGAGCCTCGCCTTT
H-β-actin-R	TCATCATCCATGGTGAGCTGG
H-TRIM11-F	GAGAACGTGAACAGGAAGGAG
H-TRIM11-R	CCATCGGTGGCACTGTAGAA

RT-PCR, reverse transcription PCR.

2.5.2 Western Blotting

Fresh tissue samples (1–2 mL) were homogenized under cryogenic conditions using a high-throughput tissue homogenizer (KZIII-F, Sevier Biotechnology, Wuhan, Hubei, China) for total protein isolation. Protein concentration was determined via a BCA assay kit (G2026-1000T; Servicebio, Wuhan, Hubei, China). Electrophoresis was performed by loading 40 µg of protein per lane onto 10% Bis-Tris gels (Invitrogen, Waltham, MA, USA) under 120 V for 90 minutes. Separated proteins were electroblotted onto 0.45 µm polyvinylidene fluoride (PVDF) membranes (Millipore, IPVH00010, Burlington, MA, USA) at 25 V for 30 minutes using a semi-dry transfer system (Trans-Blot Turbo, Bio-Rad, Hercules, CA, USA). Membranes were sequentially incubated with a rabbit polyclonal anti-TRIM11 antibody (10851-1-AP, 1:1000, Proteintech, Rosemont, IL, USA) and HRP-Goat anti Rabbit secondary antibody (5220-0336, 1:50,000, Seracare, Milford, MA, USA).

Table 2. Thirty-four cancer types and abbreviations in the TCGA database.

Cancer types	Abbreviations
Adrenocortical carcinoma	TCGA-ACC
Bladder urothelial carcinoma	TCGA-BLCA
Breast invasive carcinoma	TCGA-BRCA
Cervical squamous cell carcinoma and endocervical adenocarcinoma	TCGA-CESC
Cholangiocarcinoma	TCGA-CHOL
Colon adenocarcinoma	TCGA-COAD
Colon adenocarcinoma/rectum adenocarcinoma esophageal carcinoma	TCGA-COADREAD
Esophageal carcinoma	TCGA-ESCA
Glioblastoma multiforme	TCGA-GBM
Glioma	TCGA-GBMLGG
Head and neck squamous cell carcinoma	TCGA-HNSC
Kidney chromophobe	TCGA-KICH
Pan-kidney cohort (KICH+KIRC+KIRP)	TCGA-KIPAN
Kidney renal clear cell carcinoma	TCGA-KIRC
Kidney renal papillary cell carcinoma	TCGA-KIRP
Acute myeloid leukemia	TCGA-LAML
Brain lower grade glioma	TCGA-LGG
Liver hepatocellular carcinoma	TCGA-LIHC
Lung adenocarcinoma	TCGA-LUAD
Lung squamous cell carcinoma	TCGA-LUSC
Ovarian serous cystadenocarcinoma	TCGA-OV
Pancreatic adenocarcinoma	TCGA-PAAD
Pheochromocytoma and paraganglioma	TCGA-PCPG
Prostate adenocarcinoma	TCGA-PRAD
Rectum adenocarcinoma	TCGA-READ
Stomach adenocarcinoma	TCGA-STAD
Skin cutaneous melanoma	TCGA-SKCM
Stomach and esophageal carcinoma	TCGA-STES
Testicular germ cell tumors	TCGA-TGCT
Thyroid carcinoma	TCGA-THCA
Uterine corpus endometrial carcinoma	TCGA-UCEC
Uterine carcinosarcoma	TCGA-UCS
Acute lymphoblastic leukemia	TARGET-ALL
High-risk Wilms tumor	TARGET-WT

Chemiluminescent signals were captured using a JS-1070P imaging system, and band intensity was quantified with IP-WIN 6.0 software (Computaleta srl., Milan, Italy).

2.6 Pan-Cancer Analysis of the Expression and Prognostic Value of TRIM11

The standardized pan-cancer datasets in the TCGA, TARGET (https://ocg.cancer.gov/programs/target), and GTEx (https://gtexportal.org/home/) databases (Pan cancer (PANCAN), N = 19,131, G = 60,499) were downloaded from UCSC Xena (https://xenabrowser.net/). The expression data of TRIM11 were extracted from 34 cancer types (Table 2). In addition, TRIM11 expression profiles corresponding to the survival status were obtained from all pan-cancer datasets. Patients in all datasets were divided into high- and low-expression groups based on the median expression level of TRIM11 (cutoff value = 50%). Finally, Kaplan-Meier analysis was performed using the R packages "survminer" and "survival".

2.7 Statistical Analysis

Statistical analyses were conducted using R software version 4.0.3 (R Foundation for Statistical Computing, 2020, Vienna, Austria). Data visualization was performed using GraphPad Prism version 9.3.1 (GraphPad Software, Inc., San Diego, CA, USA), continuous variables are presented as mean ± standard deviation (SD), and significance was determined using Student's *t*-test, with a *p*-value of <0.05 considered statistically significant.

3. Results

3.1 TRIM11 was Overexpressed in CC

TRIM11 was found to be overexpressed in CC tissues in the TCGA-CESC and GSE67522 datasets ($p <$

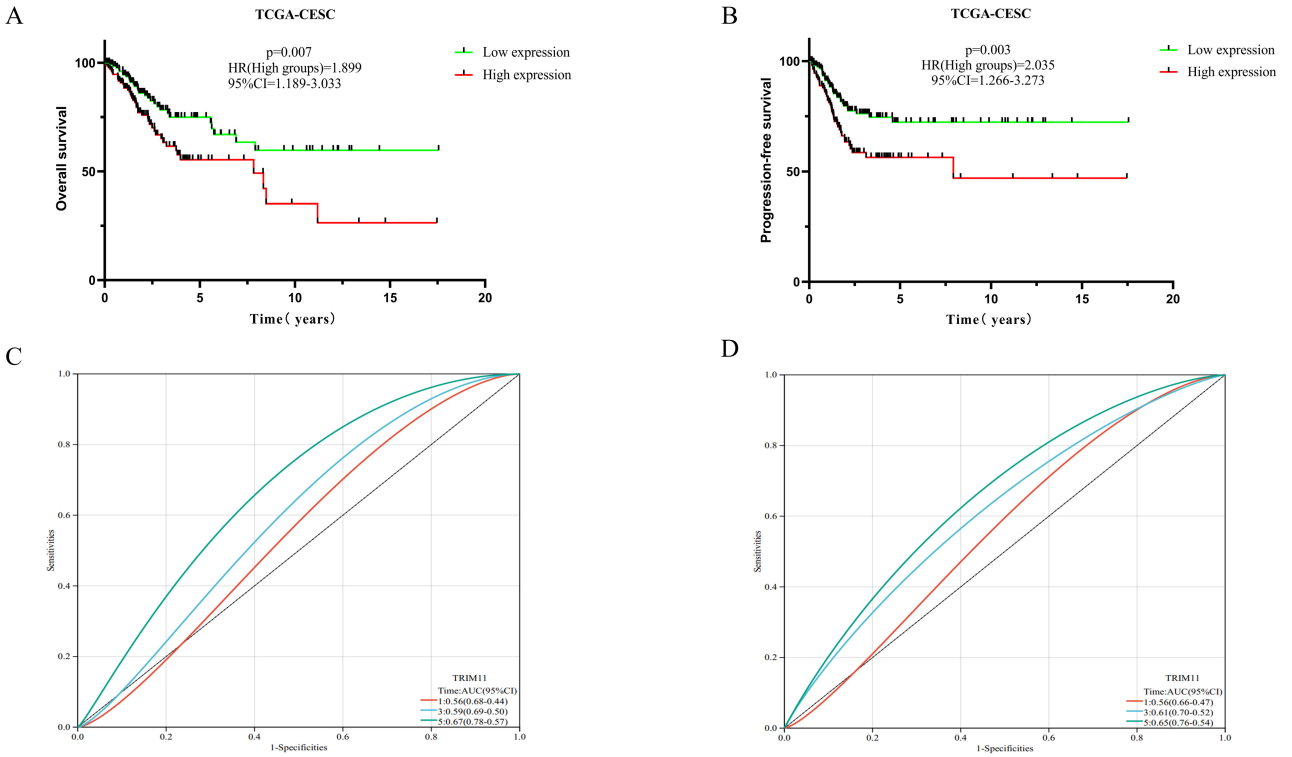

Fig. 3. Effects of TRIM11 on the prognosis of CC. (A,B) The expression of TRIM11 affected OS and PFS in CC. (C,D) ROC curves demonstrating the specificity and sensitivity of TRIM11 in predicting the 1-, 3-, and 5-year survival probabilities in CC. ROC, receiver operating characteristic; AUC, area under the ROC curve; OS, overall survival; PFS, progression-free survival.

0.0001 and $p < 0.0001$; Fig. 2A,B). Notably, the expression of TRIM11 was significantly higher in HPV-positive CC tissues than in HPV-positive normal cervical tissues ($p < 0.001$); however, no significant difference in TRIM11 expression was observed between HPV-infected and non-HPV-infected normal tissues ($p > 0.05$; Fig. 2C). Similarly, the protein and mRNA expression levels of TRIM11 were significantly higher in CC tissues than in adjacent normal tissues ($p < 0.05$ and $p < 0.05$; Fig. 2D–F).

3.2 TRIM11 Affected the Prognosis of CC

In the TCGA-CESC dataset, OS and progression-free survival (PFS) were significantly longer in patients with CC in the low-TRIM11-expression group than in those in the high-TRIM11-expression group ($p = 0.007$, HR = 1.899, 95% CI [1.189–3.033] and $p = 0.003$, HR = 2.035, 95% CI [1.266–3.273]; Fig. 3A,B). The area under the receiver operating characteristic (ROC) curve (AUC) at 1, 3, and 5 years was 0.56 ($p = 0.048$, 95% CI, 0.44–0.68), 0.59 ($p = 0.035$, 95% CI, 0.50–0.69), and 0.67 ($p = 0.012$, 95% CI, 0.57–0.78) for OS, respectively, and 0.56 ($p = 0.041$, 95% CI, 0.47–0.66), 0.61 ($p = 0.031$, 95% CI, 0.52–0.70), and 0.65 ($p = 0.022$, 95% CI, 0.54–0.76) for PFS, respectively (Fig. 3C,D).

3.3 Protein-Protein Interaction Network and GSEA of TRIM11

GSEA in the TCGA-CESC dataset showed that TRIM11 was significantly associated with various gene sets (Fig. 4), including Vascular-Smooth-Muscle-Contraction (enrichment score (ES) = 0.5834, nominal p-value (NP) = 0.0000), Tgf-Beta-Signaling-Pathway (ES = 0.5727, NP = 0.0000), Melanoma (ES = 0.5588, NP = 0.0000), Prostate-Cancer (ES = 0.5431, NP = 0.0000), Calcium-Signaling-Pathway (ES = 0.5172, NP = 0.0000), Endometrial-Cancer (ES = 0.5158, NP = 0.0000), Melanogenesis (ES = 0.4966, NP = 0.0000), WNT-Signaling-Pathway (ES = 0.4598, NP = 0.0000), Pathways-In-Cancer (ES = 0.4337, NP = 0.0000), and MAPK-Signaling-Pathway (ES = 0.4322, NP = 0.0000).

3.4 Expression and Prognostic Value of TRIM11 at the Pan-Cancer Level

No differences were observed in TRIM11 expression among the TCGA-GBM, TCGA-GBMLGG, TCGA-LGG, TCGA-KIRC, and TCGA-PCPG datasets. However, TRIM11 expression was significantly different in other cancer types. For instance, it was low in the TCGA-THCA, TCGA-TGCT, and TCGA-KICH datasets (Fig. 5A). Low expression of TRIM11 was correlated with a poor prognosis in the TCGA-GBMLGG (N = 619, $p = 1.1 \times 10^{-3}$, HR = 0.65; 95% CI, 0.50–0.84) datasets. On the contrary, high

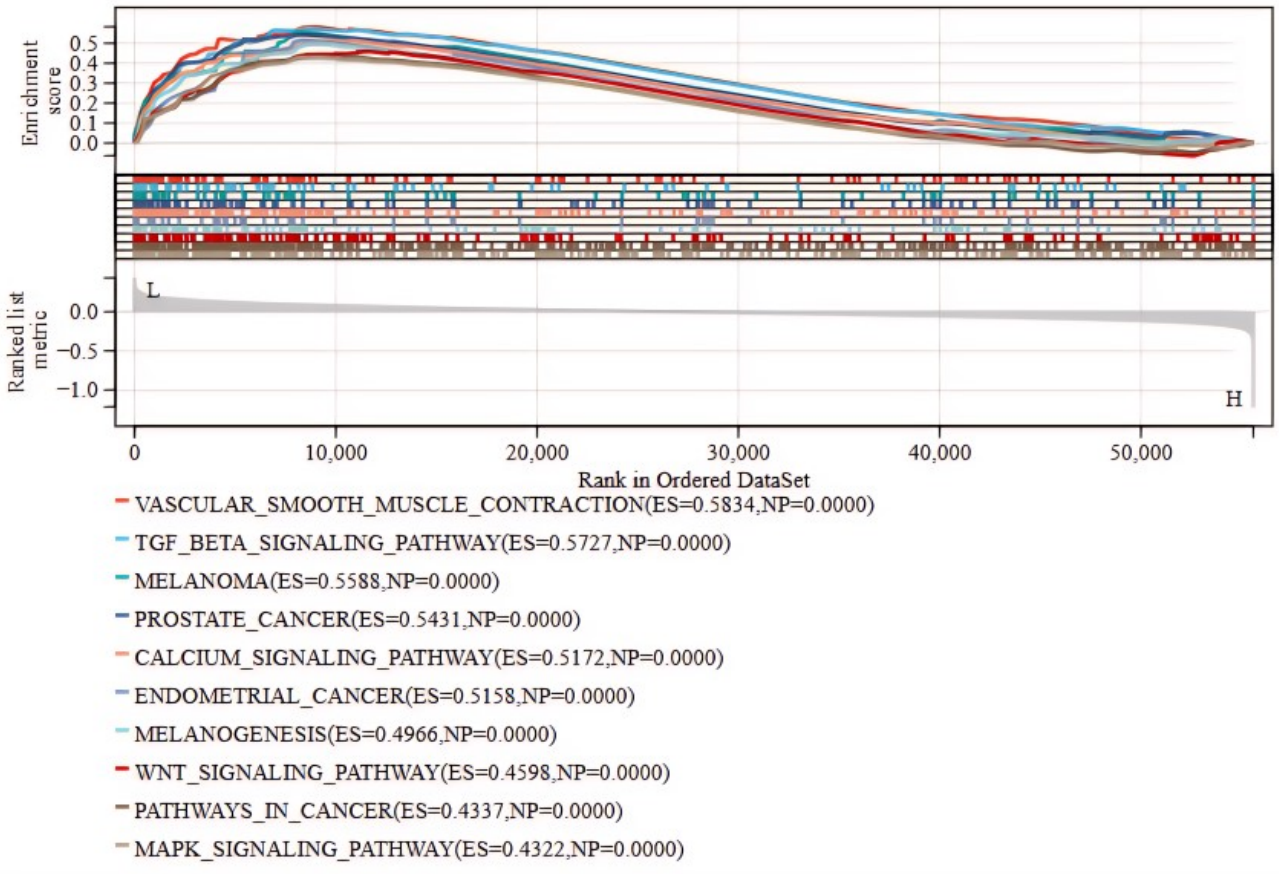

Fig. 4. Gene set enrichment analysis of TRIM11 in CC in the TCGA-CESC dataset. ES, enrichment score; NP, nominal *p*-value.

Table 3. TRIM11 affects the prognosis of pan capcer.

Cancer code	*p*-value	Hazard ratio (95% CI)
TCGA-ACC (N = 77)	2.4×10^{-4}	2.69 (1.58, 4.57)
TCGA-LAML (N = 209)	1.3×10^{-3}	1.55 (1.19, 2.03)
TCGA-LUAD (N = 490)	0.02	1.33 (1.04, 1.71)
TCGA-LIHC (N = 341)	0.02	1.32 (1.05, 1.66)
TCGA-SKCM (N = 444)	0.03	1.33 (1.02, 1.73)
TCGA-THCA (N = 501)	0.03	7.23 (1.30, 40.30)
TCGA-CESC (N = 273)	0.007	1.89 (1.19, 2.03)
TCGA-GBMLGG (N = 619)	1.1×10^{-3}	0.65 (0.50, 0.84)

expression of TRIM11 was correlated with a poor prognosis in the TCGA-LUAD (N = 490, $p = 0.02$, HR = 1.33; 95% CI, 1.04–1.71), TCGA-LIHC (N = 341, $p = 0.02$, HR = 1.32; 95% CI, 1.05–1.66), TCGA-SKCM (N = 444, $p = 0.03$, HR = 1.33; 95% CI, 1.02–1.73), TCGA-THCA (N = 501, $p = 0.03$, HR = 7.23; 95% CI, 1.30–40.30), TCGA-LAML (N = 209, $p = 1.3 \times 10^{-3}$, HR = 1.55; 95% CI, 1.19–2.03), and TCGA-ACC (N = 77, $p = 2.4 \times 10^{-4}$, HR = 2.69; 95% CI, 1.58–4.57) datasets (Fig. 5B and Table 3).

4. Discussion

In recent years, the average age of onset for CC has gradually decreased, with the incidence of CC showing an increasing trend in younger age groups [16]. The development of CC can be effectively controlled through the early examination and prompt treatment of precancerous lesions [17]. Therefore, identifying novel biomarkers closely related to the development of CC is necessary.

As a pivotal member of the TRIM family, TRIM11 has emerged as a promising diagnostic biomarker across malignancies [18]. Our investigation revealed pronounced TRIM11 overexpression in cervical cancer (CC) tissues, correlating with extended PFS and OS in affected patients. Complementary evidence from Zhang *et al.* [19] demonstrated elevated TRIM11 expression in SiHa and HeLa CC cell lines, where genetic silencing substantially attenuated cellular proliferation, migration, and invasion—underscoring its therapeutic potential. Mechanistic studies implicate TRIM11 in protein kinase B (AKT) pathway hyperactivation, thereby driving CC progression. This aligns with our observations of concordant TRIM11 upregulation at both transcriptomic (mRNA) and proteomic levels in clinical CC specimens. Notably, while TRIM proteins are recognized for their antiviral roles [20], TRIM11 exhibits paradoxical immunomodulatory functions. Interferons (IFNs), central to antiviral defense and cellular regulation [21], are counterintuitively suppressed by TRIM11 via inhibition of interferon-beta (IFN-β) production and ac-

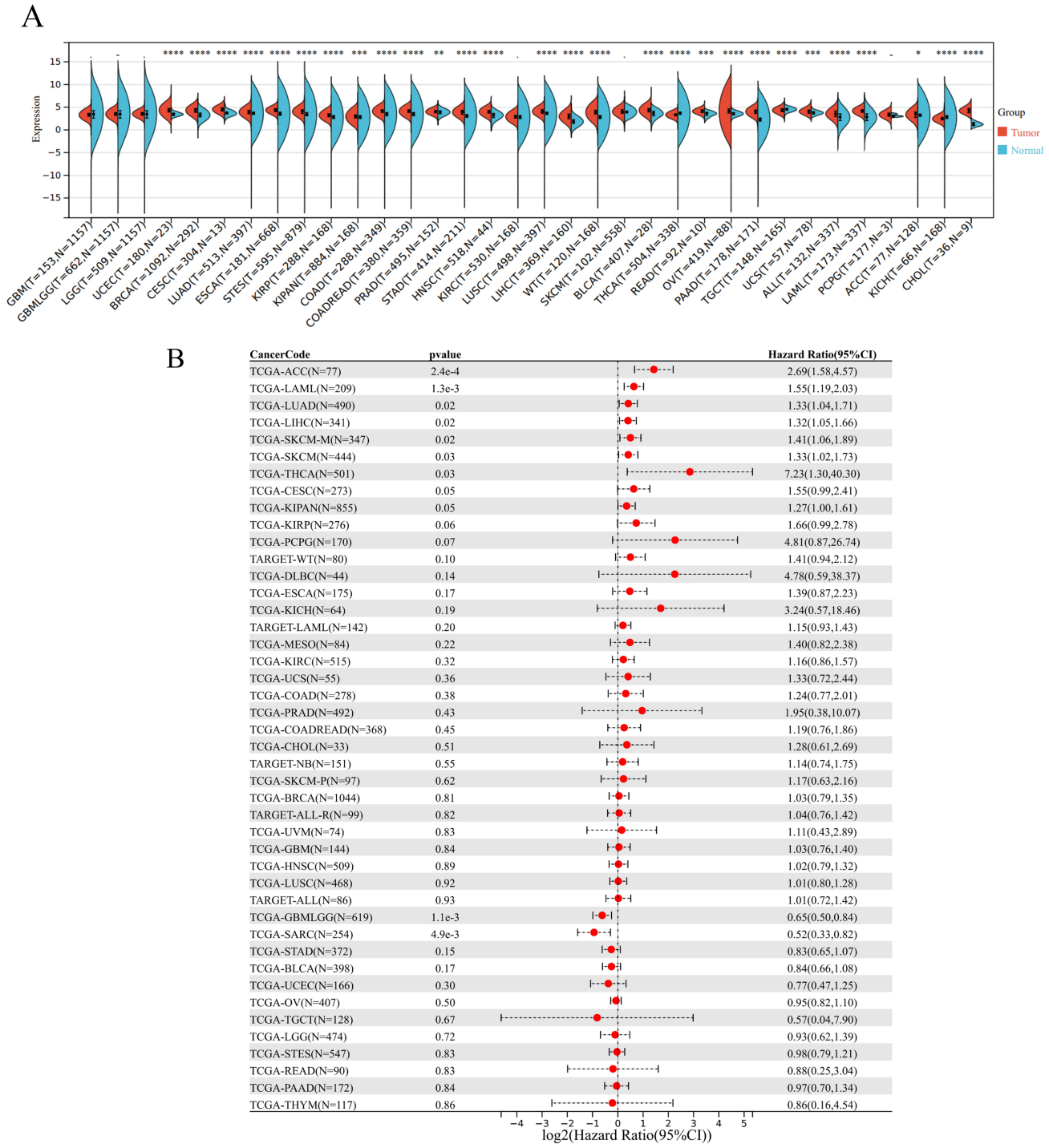

Fig. 5. Pan-cancer analysis of the expression level and prognostic value of TRIM11. (A) Pan-cancer expression of TRIM11 (*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$). (B) Pan-cancer prognostic value of TRIM11.

tivity [22]. Our data further delineate a tumor-specific regulatory axis: HPV-positive CC tissues displayed orders-of-magnitude higher TRIM11 expression compared to HPV-infected normal epithelia ($p < 0.001$), whereas no differential expression was detected between HPV-positive and HPV-negative normal tissues. Collectively, these findings posit TRIM11 as a dual-faceted driver of CC pathogenesis, operating through oncogenic AKT signaling and IFN-mediated immune evasion. Based on these findings, we speculate that TRIM11 promotes the development of CC and affects the prognosis. The potential mechanism through which TRIM11 contributes to CC is the negative regulation of IFN.

GSEA showed that TRIM11 was closely related to the TGF-β, calcium, and MAPK signaling pathways in CC. Recently, TGF-β has been identified as a promising therapeutic target for CC. In advanced CC, TGF-β enhances metastasis, cancer stem cell viability, drug resistance, and immune evasion, thereby promoting tumor development. Blockade of TGF-β can effectively improve treatment efficacy, especially in immunotherapy [23]. Ca^{2+} signaling has been shown to promote the growth, proliferation, and metastasis of CC. Mechanistically, regulating various Ca^{2+} channels, pumps, exchangers, sensors, and activation effectors can affect the concentration of Ca^{2+} both inside and outside the cell [24]. The MAPK signaling pathway plays an important role in physiological activities such as cell proliferation, differentiation, apoptosis, and angiogenesis in mammals. In CC, abnormal activation of the MAPK pathway is closely associated with the proliferative, invasive, and metastatic abilities of CC cells [25].

This investigation corroborates prior findings demonstrating tumor-specific TRIM11 dysregulation across malignancies, with marked expression disparities between neoplastic and matched normal tissues. Accumulating evidence positions TRIM11 as a pan-cancer prognostic modulator, exhibiting tissue-specific oncogenic behaviors: Lung Cancer: elevated TRIM11 levels correlate with advanced TNM staging, tumor dimensions, lymph node involvement, and reduced overall survival [26]. Breast Cancer: TRIM11 upregulation drives unchecked cellular proliferation through cell cycle deregulation [27]. Thyroid Cancer: in anaplastic thyroid carcinoma (ATC), TRIM11 silencing attenuates proliferative/migratory capacities and enhances chemosensitivity [28]. Glioma: high-grade gliomas exhibit TRIM11-driven malignant progression via enhanced invasion and treatment resistance, particularly temozolomide (TMZ) in glioblastoma (GBM) [29]. Hepatocellular Carcinoma (HCC): pathological TRIM11 overexpression sustains HCC aggressiveness, whereas its suppression impedes proliferation and metastatic potential [24]. These collective findings establish TRIM11 as a multifaceted therapeutic target, with mechanistic diversity spanning proliferation modulation, treatment resistance, and metastatic programming. In addition, TRIM11 was found to inhibit the PI3K/AKT signaling pathway in HCC cells. These findings suggest that TRIM11 plays an important role in the progression of HCC and serves as a promising therapeutic target for this disease. In this study, we found that in TCGA-GBMLGG and TRIM11 exhibited HRs <1, suggesting tumor-suppressive properties. Conversely, elevated HRs (>1) were observed in TCGA-ACC, TCGA-LAML, TCGA-LUAD, TCGA-LIHC, TCGA-SKCM, TCGA-CESC, and TCGA-THCA, implicating TRIM11 as a risk factor in these malignancies.

However, this study has its limitations: (1) small sample size: the study used limited cervical cancer samples from public datasets and only validated results in four tissue pairs, which may reduce reliability. (2) Lack of mechanism validation: while TRIM11 was linked to key pathways (such as TGF-β and MAPK), functional experiments to confirm its role were not performed. (3) HPV subtype analysis missing: TRIM11's association with high-risk HPV subtypes (e.g., HPV16/18) was not explored. (4) Pan-cancer variability: TRIM11's prognostic role across 34 cancer types requires deeper validation due to differences in cancer biology. In the following research, we will investigate the functionality of TRIM11 in CC.

5. Conclusions

TRIM11 is overexpressed in cervical cancer and linked to poor survival, potentially driving progression via pathways like TGF-β and MAPK. Its role as a biomarker across cancers highlights broad relevance, but larger studies and mechanistic experiments are needed for validation and therapeutic development.

Availability of Data and Materials

Data related to this study are available by requesting the corresponding author via e-mail.

Author Contributions

GZ, HC, and YT designed the research study. GZ performed the research. HC and YT provided help and advice on the qRT-PCR Western blotting experiments. HC analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. Formal ethical authorization for this investigation was secured from the Institutional Review Board of Zhuzhou Central Hospital (Ethics Approval Code: 20231046). Prior to enrollment, all eligible individuals provided documented informed consent in accordance with institutional protocols.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Pimple S, Mishra G. Cancer cervix: Epidemiology and disease burden. Cytojournal. 2022; 19: 21. https://doi.org/10.25259/CMAS_03_02_2021.

[2] Singh D, Vignat J, Lorenzoni V, Eslahi M, Ginsburg O, Lauby-Secretan B, *et al*. Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the who Global Cervical Cancer Elimination Initiative. The Lancet Global Health. 2023; 11: e197–e206. https://doi.org/10.1016/S2214-109X(22)00501-0.

[3] Koh WJ, Abu-Rustum NR, Bean S, Bradley K, Campos SM, Cho KR, *et al*. Cervical cancer, version 3.2019, NCCN clinical practice guidelines in oncology. Journal of the National Comprehensive Cancer Network. 2019; 17: 64–84. https://doi.org/10.6004/jnccn.2019.0001.

[4] Li T, Zhang H, Lian M, He Q, Lv M, Zhai L, *et al*. Global status and attributable risk factors of breast, cervical, ovarian, and uterine cancers from 1990 to 2021. Journal of Hematology & Oncology. 2025; 18: 5. https://doi.org/10.1186/s13045-025-01660-y.

[5] Cervical cancer causes, risk factors, and prevention: patient version. PDQ Cancer Information Summaries [Internet]. Patient version. National Cancer Institute: US. 2024.

[6] Luvián-Morales J, Gutiérrez-Enríquez SO, Granados-García V, Torres-Poveda K. Risk factors for the development of cervical cancer: analysis of the evidence. Frontiers in Oncology. 2024; 14: 1378549. https://doi.org/10.3389/fonc.2024.1378549.

[7] Fowler JR, Maani EV, Dunton CJ, Gasalberti DP, Jack BW, Miller JL. Cervical Cancer. StatPearls Publishing [Internet]: Treasure Island. 2023.

[8] Musunuru HB, Pifer PM, Mohindra P, Albuquerque K, Beriwal S. Advances in management of locally advanced cervical cancer. Indian Journal of Medical Research. 2021; 154: 248–261. https://doi.org/10.4103/ijmr.IJMR_1047_20.

[9] Castellano T, Ding K, Moore KN, Landrum LM. Simple hysterectomy for cervical cancer: risk factors for failed screening and deviation from screening guidelines. Journal of Lower Genital Tract Disease. 2019; 23: 124–128. https://doi.org/10.1097/LGT.0000000000000463.

[10] Wang Z, Xu X, Tang W, Zhu Y, Hu J, Zhang X. Tripartite motif containing 11 interacts with DUSP6 to promote the growth of human osteosarcoma cells through regulating ERK1/2 pathway. BioMed Research International. 2019; 2019: 1–10. https://doi.org/10.1155/2019/9612125.

[11] Hatakeyama S. TRIM family proteins: roles in autophagy, immunity, and carcinogenesis. Trends in Biochemical Sciences. 2017; 42: 297–311. https://doi.org/10.1016/j.tibs.2017.01.002.

[12] Yang L, Xia H. TRIM Proteins in inflammation: from expression to emerging regulatory mechanisms. Inflammation. 2021; 44: 811–820. https://doi.org/0.1007/s10753-020-01394-8.

[13] Shen Z, Wei L, Yu ZB, Yao ZY, Cheng J, Wang YT, *et al*. The roles of trims in antiviral innate immune signaling. Front Cell Infect Microbiol. 2021; 11: 628275. https://doi.org/10.3389/fcimb.2021.628275.

[14] Pan Y, Yu H, Lu F. TRIM11 posttranscriptionally modulated by miR-5193 facilitates tumor growth and metastasis of prostate cancer. Technology in Cancer Research & Treatment. 2023; 22. https://doi.org/10.1177/15330338231178639.

[15] Kuempers C, Jagomast T, Paulsen FO, Heidel C, Bohnet S, Schierholz S, *et al*. TRIM11 expression in non-small cell lung cancer is associated with poor prognosis. Histology and Histopathology. 2024; 39: 437–446. https://doi.org/10.14670/HH-18-647.

[16] Li X, Zheng R, Li X, Shan H, Wu Q, Wang Y, *et al*. Trends of incidence rate and age at diagnosis for cervical cancer in China, from 2000 to 2014. Chinese Journal of Cancer Research. 2017; 29: 477–486. https://doi.org/10.21147/j.issn.1000-9604.2017.06.02.

[17] yadav G, Srinivasan G, jain A. Cervical cancer: Novel treatment strategies offer renewed optimism. Pathology-Research and Practice. 2024; 254: 155136. https://doi.org/10.1016/j.prp.2024.155136.

[18] Chen L, Zhu G, Johns EM, Yang X. TRIM11 activates the proteasome and promotes overall protein degradation by regulating USP14. Nature Communications. 2018; 9: 1223. https://doi.org/10.1038/s41467-018-03499-z.

[19] Zhang P, Tang Y, Zhao J, Yang J, Chen Y, Gong Y, *et al*. TRIM11 regulated by m6a modification promotes the progression of cervical cancer by PHLPP1 ubiquitination. Neoplasma. 2023; 70: 659–669. https://doi.org/10.4149/neo_2023_230104N7.

[20] van Gent M, Sparrer KMJ, Gack MU. TRIM Proteins and their Roles in Antiviral Host Defenses. Annual Review of Virology. 2018; 5: 385–405. https://doi.org/10.1146/annurev-virology-092917-043323.

[21] Walter MR. The role of structure in the biology of interferon signaling. Frontiers in Immunology. 2020; 11: 606489. https://doi.org/10.3389/fimmu.2020.606489.

[22] Lee Y, Song B, Park C, Kwon KS. TRIM11 negatively regulates IFNβ production and antiviral activity by targeting TBK1. PLOS One. 2013; 8: e63255. https://doi.org/10.1371/journal.pone.0063255.

[23] Yin S, Cui H, Qin S, Yu S. Manipulating TGF-β signaling to optimize immunotherapy for cervical cancer. Biomedicine & Pharmacotherapy. 2023; 166: 115355. https://doi.org/10.1016/j.biopha.2023.115355.

[24] Lei J, Deng F, Ding H, Fu M, Xu T, Ji B, *et al*. Recent developments on the roles of calcium signals and potential therapy targets in cervical cancer. Cells. 2022; 11: 3003. https://doi.org/10.3390/cells11193003.

[25] Hu Z, Wang H, Fu Y, Ma K, Ma X, Wang J. Gentiopicroside inhibits cell growth and migration on cervical cancer via the reciprocal MAPK/Akt signaling pathways. Nutrition and Cancer. 2021; 73: 1459–1470. https://doi.org/10.1080/01635581.2020.1801777.

[26] Liang Z, Li J, Zhang G, Chen M. TRIM11 promotes cell proliferation of non-small cell lung cancer through the inhibition of ferroptosis by AMPK. The Clinical Respiratory Journal. 2023; 17: 1006–1016. https://doi.org/10.1111/crj.13675.

[27] Song W, Wang Z, Gu X, Wang A, Chen X, Miao H, *et al*. TRIM11 promotes proliferation and glycolysis of breast cancer cells via targeting AKT/GLUT1 pathway. OncoTargets and Therapy. 2019; 12: 4975–4984. https://doi.org/10.2147/OTT.S207723.

[28] Tang J, Tian Z, Liao X, Wu G. SOX13/TRIM1/YAP axis promotes the proliferation, migration and chemoresistance of anaplastic thyroid cancer. International Journal of Biological Sciences. 2021; 17: 417–429. https://doi.org/10.7150/ijbs.54194.

[29] Di K, Abrams D, Yadav P, Das B, Bota D. EXTH-50. Identifying TRIM11 as a Potential therapeutic target for malignant gliomas. Neuro-Oncology. 2022; 24: vii220–vii220. https://doi.org/10.1093/neuonc/noac209.848.