Phosphoglycerate-kinase-1 Is a Potential Prognostic Biomarker in HNSCC and Correlates With Immune Cell Infiltration

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Abstract. Background/Aim: Head and neck squamous cell carcinoma (HNSCC) is the sixth leading cancer worldwide, with a high recurrence rate and a low cure rate. Phosphoglycerate kinase 1 (PGK1), an essential enzyme in the aerobic glycolysis pathway, is a prognostic marker for a variety of cancers. However, it remains unclear whether a PGK1-based immune signature can be used as a prognostic biomarker in HNSCC patients. Materials and methods: We explored the potential oncogenic mechanisms of PGK1 by multiple bioinformatics analyses combined with multiple databases, including the correlation between PGK1 and prognosis, and the infiltration of immune cells in HNSCC. Functional enrichment analyses were further performed to investigate the potential role of PGK1 in HNSCC. Results: The expression of PGK1 was significantly higher in HNSCC tissues compared to normal tissues. High expression of PGK1 was associated with poor prognosis in HNSCC, and multivariate cox regression analysis showed that PGK1 could be an independent prognostic factor in HNSCC. Pathway analysis revealed that PGK1 may regulate the pathogenesis of HNSCC through the immune signaling pathway. Moreover, PGK1 expression significantly correlated with the infiltration level of 16 types of immune cells. Conclusion: The current study reports that PGK1 expression was increased in HNSCC and that high PGK1 expression was closely associated with poor prognosis and immune cell infiltration, which could serve as a promising independent prognostic biomarker and potential immunotherapeutic target for HNSCC.

Head and neck squamous cell carcinoma (HNSCC) is the sixth leading cancer worldwide, arising from the oral cavity, pharynx, larynx, and hypopharynx (1). The global mortality rate of HNSCC is ranked 12th, with approximately 840,000 cases in 2020, which is expected to rise to 1 million by 2030 (2). Despite technological advancements in the treatment of HNSCC, its overall survival and prognosis remain poor, with a five-year overall survival rate of 50% (3, 4); a large number of patients die of metastasis, immune suppression and recurrence (5). Therefore, it is urgent to discover more sensitive and specific molecular markers to improve the early diagnosis and targeted treatment of HNSCC.

Notably, cancer cells show extensive enhancement of aerobic glycolysis, including overexpression of glycolytic enzyme and an increase in lactate production (6, 7). Phosphoglycerate kinase 1 (PGK1) is an essential enzyme of aerobic glycolysis (8). It catalyzes the reversible transfer of a phosphate group from 1,3-bisphosphoglycerate to adenosine diphosphate (ADP) and produces 3-phosphoglycerate and adenosine triphosphate (ATP) (9). Previous studies have confirmed that PGK1 was associated with poor prognosis of several types of cancer; it also has a higher expression in tumors than that in the normal tissues (8, 10). In cellular experiments, overexpression of PGK1 promotes tumor cell proliferation, migration and invasion (11, 12). In the nucleus, PGK1 preferentially drives cell metastasis via mitochondrial oxidative phosphorylation induction, whereas cytoplasmic PGK1 preferentially supports proliferation by functioning as a glycolytic enzyme in SMAD4-negative pancreatic ductal adenocarcinoma (12). Concerning its molecular mechanism, the overexpression of PGK1 was correlated with mutations of the tumor suppressor genes tumor suppressor p53 (TP53) and E-cadherin (CDH1), while the acetylation at the K323 site of PGK1 was found to be a key regulatory mechanism for...
promoting its enzymatic activity and cancer cell metabolism in breast and liver cancer (13, 14). Similarly, the depletion of PGK1 dramatically reduced cancer cell proliferation and tumorigenesis (8, 14). Recently, it has been documented that PGK1 was associated with hypoxia and immune regulation, resulting in the promotion of glycolysis, enhancing stem cell-like properties and epithelial-mesenchymal transition (EMT) by activating protein kinase B (AKT) signaling in oral squamous cell carcinoma (OSCC) (15-17). However, whether the PGK1-based immune signature could serve as a prognostic biomarker for patients with HNSCC remains unclear.

This study identified the expression levels of PGK1 in HNSCC and its correlation with the prognosis of HNSCC patients by applying multiple bioinformatics analyses. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses and Gene set enrichment analyses (GSEA) were applied to investigate the potential function of PGK1 in HNSCC. In addition, we investigated the correlation of PGK1 with different levels of immune cell infiltration and further evaluated the predictive performance of PGK1 for high infiltration levels of HNSCC.

Materials and Methods

Datasets and data preprocessing. We explored the differential expression of PGK1 in HNSCC and normal tissues based on The Cancer Genome Atlas (TCGA) dataset using the Tumor immune estimation resource, version 2.0 (TIMER2.0) online tool (http://timer.cistrome.org/) (18), and Gene expression profiling interactive analysis, version 2.0 (GEPIA2.0) online tool (http://gepia2.cancer-pku.cn) (19). The expression levels of total protein of PGK1 between primary tumor and normal tissues were investigated using the clinical proteomic tumor analysis consortium (CPTAC) dataset in the UALCAN tool (http://ualcan.path.uab.edu/index.html) (20).

Human protein atlas (HPA). Images of immunohistochemistry staining for HNSCC (https://www.proteinatlas.org/ENSG0000102144-PGK1/pathology/head-and-neck-cancer#img) and normal salivary gland tissues (https://www.proteinatlas.org/ENSG0000102144-PGK1/tissue/salivary-gland#img) were collected from the human protein atlas (HPA, HPA045385). HPA applies transcriptome and proteomics to provide different protein atlases, including tissue, cell, and pathology atlases (21).

Correlations between PGK1 and survival in HNSCC. We extracted survival information for each sample in the TCGA database and then selected overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) data for PGK1 in HNSCC to investigate the association between PGK1 expression and the prognosis of HNSCC patients. Kaplan-Meier (KM) and log-rank tests were performed for survival analysis of HNSCC (p<0.05), and survival curves were analyzed using the R packages “survminer v0.4.9” (https://CRAN.R-project.org/package=survminer) and “survival v3.5-7” (https://cran.r-project.org/web/packages/survival). Identification of the prognostic factors for OS in HNSCC. Cox regression analysis was used to evaluate the prognostic factors. Multivariate Cox analysis and univariate Cox regression were adopted to compare the impact of PGK1 expression on survival along with other clinical features. The median PGK1 expression was regarded as the cut-off value. A p-value <0.05 was considered statistically significant. Moreover, receiver operating characteristic (ROC) analysis was performed to assess the effectiveness of the transcriptional expression of PGK1 in distinguishing HNSCC from healthy samples. The computed area under the curve (AUC) value ranging from 0.5 to 1.0 indicated an excellent predictive value.

PGK1-related gene enrichment analysis. We analyzed the 570 significant differential genes related to the PGK1 gene in HNSCC by Gene Ontology (GO) functional analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis. GO functional analysis comprising cellular component (CC), molecular function (MF), and biological process (BP), as well as KEGG pathway analysis, were implemented using the ClusterProfiler v3.6.0 package (22) in R. GSEA was used to enrich 10 significant KEGG pathways. The gene set was permuted 1,000 times for each analysis. An adjusted p-value <0.05 was considered to be statistically significant.

Relationship between PGK1 and immune cell infiltration. We used TCGA data to quantify the relative abundance of tumor-infiltrating immune cells in HNSCC patients using the single-sample gene set enrichment analysis (ssGSEA) algorithm (23) in the R package GSVA (24), containing 24 gene sets labeling different tumor-infiltrating immune cell types [aDC (activated dendritic cells), B cells, CD8 T cells, cytotoxic cells, DC (dendritic cells), eosinophils, immature dendritic cells (iDC), macrophages, mast cells, neutrophils, NK CD56bright cells, NK CD56dim cells, NK cells, plasmacytoid dendritic cells (pDC), T cells, T central memory (Tcm), T effector memory (Tem), T follicular helper (TFH), T gamma delta (Tgd), T helper cells, Type 1 T helper (Th1) cells, Type 17 T helper (Th17) cells, Type 2 T helper (Th2) cells, regulatory T cells (Treg)], to comprehensively study the molecular characteristics of tumor-immune interactions in HNSCC. To examine the association between PGK1 expression and the abundance of tumor-infiltrating immune cells, enrichment scores characterized the degree of infiltration of each type of immune cells in the samples, and p-values were calculated using the Wilcoxon rank-sum and Spearman’s rank correlation tests.

Results

Elevated expression of PGK1 in HNSCC and normal tissues. To explore the possible role of PGK1 in carcinogenesis, we first analyzed the expression of PGK1 in 33 human cancers from the TCGA dataset using the TIMER2.0 online tool. As shown in Figure 1A, PGK1 was significantly overexpressed in 16 cancers compared with normal samples, including bladder urothelial carcinoma (BLCA), breast invasive carcinoma (BRCA), cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC), cholangiocarcinoma (CHOL), colon adenocarcinoma (COAD), esophageal carcinoma (ESCA), glioblastoma multiforme (GBM), head and neck squamous cell carcinoma (HNSC), kidney renal clear cell carcinoma (KIRC), liver hepatocellular carcinoma (LIHC), lung adenocarcinoma.
Figure 1. Phosphoglycerate kinase 1 (PGK1) was upregulated and had prognostic value in head and neck squamous cell carcinoma (HNSCC). (A) The expression of the PGK1 gene in HNSCC from the cancer genome atlas (TCGA) data. (B) PGK1 expression levels in HNSCC and matched normal tissues. (C) Receiver operating characteristic (ROC) analysis of PGK1 showed promising discrimination power between tumor and normal tissues. (D) The protein levels of PGK1, based on the Human Protein Atlas.
(LUAD), lung squamous cell carcinoma (LUSC), prostate adenocarcinoma (PRAD), rectum adenocarcinoma (READ), stomach adenocarcinoma (STAD), and uterine corpus endometrial carcinoma (UCEC). We further compared the expression of PGK1 in 41 cancer tissues with paired normal tissues, and the result illustrated that PGK1 was significantly overexpressed in tumors (Figure 1B). In addition, ROC curves were used to evaluate the feasibility of distinguishing tumors from normal tissues based on the expression level of PGK1, and the results indicated that PGK1 had a certain accuracy (AUC=0.888) in predicting HNSCC (Figure 1C). Moreover, immunohistochemical staining from HPA also revealed that PGK1 protein was upregulated in HNSCC tissue (Figure 1D).

**Association between PGK1 expression and cancer patient survival prognosis.** We performed univariate and multivariate Cox analysis of overall survival to explore PGK1 as an independent prognostic factor of HNSCC. In the univariate Cox analysis model, N stage [hazard ratio (HR)=1.367, \( p=0.029 \)], M stage (HR=4.794, \( p=0.002 \)), and PGK1 expression (HR=1.76, \( p<0.001 \)) were significantly associated with OS in HNSCC patients. In the multivariate Cox analysis model, N stage (HR=1.362, \( p=0.040 \)), M stage (HR=4.179, \( p=0.005 \)), and PGK1 (HR=1.838, \( p<0.001 \)) were still relevant to worse prognosis (Table I).

Furthermore, we investigated the relationship between PGK1 expression and overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) in HNSCC patients. According to the KM plot, high PGK1 expression was positively correlated with poor OS [HR=1.76, 95% confidence interval (CI)=1.34-2.32, \( p<0.001 \), Figure 2A], poor DSS (HR=2.15, 95% CI=1.49-3.10, \( p<0.001 \), Figure 2B), and poor PFI (HR=1.63, 95% CI=1.22-2.18, \( p=0.001 \), Figure 2C). The KM Plotter database analysis showed that the PGK1 expression level has a significant impact on OS of patients (HR=2.13, logrank \( p=0.0049 \), Figure 2D). These results indicate that PGK1 expression is a risk factor for prognosis in patients with HNSCC.

**Identification of differentially expressed genes in HNSCC samples with low and high PGK1 expression.** The TCGA database was used to analyze the differences between the PGK1 high- and low-expression groups’ gene expression profiles. We sorted the PGK1 expression of all samples from low to high, with the first 0-50% of samples as the PGK1 low expression group, and the last 50-100% of samples as the PGK1 high expression group. DESeq2 (v1.18.0) was used to identify differentially expressed genes (DEGs) between the PGK1 high- and low-expression groups and a total of 570 DEGs, including 70 up-regulated and 500 down-regulated, were identified as statistically significant (log fold change (logFC) >1, \( p<0.05 \)) (Figure 3A). We explored significant genes associated with PGK1 in HNSCC using TCGA data and identified 10,951 significant co-expressed genes, of which 8,758 were positively related and 2,193 were negatively related to PGK1. The heat map displayed the top five positively related DEGs and top five negatively related DEGs between PGK1 high- and PGK1 low-expressed groups (Figure 3B). We found that the genes most positively associated with PGK1 included P4HA1, LDHA, PDK1, NDRG1, and PFKP, while those negatively associated with PGK1 included TMEM125, ACKR1, COX4I2, CLEC3B, and SPNS3.

**Functional analysis of PGK1.** We analyzed 570 differentially expressed genes between high and low expression of PGK1 in HNSCC. GO and KEGG functional enrichment analysis was performed by the clusterProfiler package. Biological process (BP) of GO enrichment analysis showed that epidermal cell differentiation, keratinocyte differentiation and muscle contraction were significantly enriched (Figure 4A). Cellular components (CC) of the GO enrichment analysis

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**Table I.** Univariate and multivariate analysis of clinicopathological factors that correlate with overall survival (OS) of head and neck squamous cell carcinoma (HNSCC) patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (N)</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Hazard ratio (95% CI)</td>
<td>( p )-Value</td>
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<tr>
<td>T stage (T1&amp;T2 vs. T3&amp;T4)</td>
<td>484</td>
<td>1.230 (0.921-1.642)</td>
<td>0.160</td>
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<tr>
<td>N stage (N0&amp;N1 vs. N2&amp;N3)</td>
<td>477</td>
<td>1.376 (1.033-1.833)</td>
<td>0.029</td>
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<tr>
<td>M stage (M0 vs. M1)</td>
<td>474</td>
<td>4.794 (1.765-13.016)</td>
<td>0.002</td>
</tr>
<tr>
<td>Sex (Male vs. Female)</td>
<td>499</td>
<td>0.754 (0.566-1.004)</td>
<td>0.054</td>
</tr>
<tr>
<td>Age (≤60 vs. &gt;66)</td>
<td>499</td>
<td>0.808 (0.617-1.058)</td>
<td>0.122</td>
</tr>
<tr>
<td>Smoker (Yes vs. No)</td>
<td>489</td>
<td>1.085 (0.775-1.520)</td>
<td>0.633</td>
</tr>
<tr>
<td>PGK1 (Low vs. High)</td>
<td>499</td>
<td>1.760 (1.337-2.317)</td>
<td>(&lt;0.001)</td>
</tr>
</tbody>
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PGK1: Phosphoglycerate kinase 1. Bold values indicate statistical significance.
showed that contractile fiber, myofibril and contractile fiber part were mainly enriched (Figure 4B). Molecular function (MF) of GO enrichment analysis showed that receptor ligand activity, peptidase regulator activity and peptidase inhibitor activity were prominently enriched (Figure 4C). KEGG enrichment analysis demonstrated that adrenergic signaling in cardiomyocytes was the most significantly enriched pathway, and primary immunodeficiency was also a crucial pathway (Figure 4D). Next, Gene Set Enrichment Analysis (GSEA) analysis was conducted to gain further insight into the biological pathways involved in HNSCC with different PGK1 expression levels. The results showed that high PGK1 expression was mainly enriched in primary immunodeficiency, graft versus host disease, allograft rejection, asthma, and linoleic acid metabolism-related signaling pathways (Figure 4E). Notably, we found primary immunodeficiency in both the KEGG and GSEA result; thus, we speculated that these genes were associated with immunity.
The previous enrichment analysis revealed that PGK1 was mainly related to primary immunodeficiency. We surmised that there might be some relationship between PGK1 and immune cells. Thus, we furtherly investigated the association between PGK1 expression and immune infiltration in HNSCC by calculating the correlation between PGK1 and 24 immune-cell subsets via the means of ssGSEA with Spearman’s r (Figure 5A). In this regard, PGK1 was shown to be significantly correlated with 16 immune cell types, including positive correlations with the level of infiltration of Th2 cells (r=0.222, p<0.001, Figure 5B), Tcm (r=0.109, p=0.015, Figure 5C), Tgd (r=0.095, p=0.034, Figure 5D), and negatively correlated with the level of infiltration of NK CD56 bright cells (r=−0.213, p<0.001, Figure 5E), NK cells (r=−0.090, p=0.045, Figure 5F), Th17 cells (r=−0.121, p=0.007, Figure 5G), Treg (r=−0.133, p=0.003, Figure 5H), TFH (r=−0.142, p=0.001, Figure 5I), TEM (r=−0.145, p=0.001, Figure 5J), DC (r=−0.153, p<0.001, Figure 5K), Mast cells (r=−0.178, p<0.001, Figure 5L), T cells (r=−0.185, p<0.001, Figure 5M), cytotoxic cells (r=−0.203, p<0.001, Figure 5N), CD8 T cells (r=−0.211, p<0.001, Figure 5O), B cells (r=−0.258, p<0.001, Figure 5P) and pDC (r=−0.344, p<0.001, Figure 5Q). These results revealed that PGK1 may play an integral role in regulating lymphocyte infiltration in HNSCC, which prompted us to further investigate the association between PGK1 expression levels and immune infiltration. Astonishingly, we found significant differences in the levels of infiltrating immune cells when PGK1 expression was divided into high and low groups, including Th2 cells, NK CD56 bright cells, T cells, cytotoxic cells, CD8 T cells, B cells and pDC (Figure 6A, D, L-P, p<0.001), Th17 cells, Treg, TFH, TEM, DC and mast cells (Figure 6F-K, p<0.01), while no significant differences were found regarding Tcm, Tgd and NK cells (Figure 6B-C, E). To verify this result, we set a decreased cellular content of Th2 cells in the KM Plotter database and found that PGK1 does not have a significant impact on OS in HNSCC patients (HR=4.13, logrank p=0.094, Figure 7), indicating the importance of the effect of Th2 cells on PGK1.

**Discussion**

HNSCC is the sixth most common cancer in humans and the prognosis is still rather poor (25). It is necessary to find more accurate biomarkers for detection at an early stage and for better monitoring cancer progression. In recent years, an increasing number of studies has shown that PGK1 is overexpressed in various cancer types, and the inhibition of PGK1 could suppress tumor growth and metastasis (26, 27). Many cancer cells display enhanced glycolysis and suppressed mitochondrial metabolism; PGK1 is an ATP-producing enzyme involved in the first ATP-generating step of the glycolytic pathway. PGK1 promotes tumorigenesis and progression by mediating glycolysis that generates ATP for tumor cells, especially under hypoxic conditions (28, 29). To date, few studies have explored the relationship between PGK1 and HNSCC (30).

In this study, we attempted to explore the potential mechanism of PGK1 in promoting HNSCC and its feasibility...
Figure 4. Functional analysis of phosphoglycerate kinase 1 (PGK1). (A) Gene ontology (GO) enrichment analysis in the biological process (BP) category. (B) GO enrichment analysis in the molecular function (MF) category. (C) GO enrichment analysis in the cellular component (CC) category. (D) Kyoto encyclopedia of genes and genomes (KEGG) pathway enrichment analysis. (E) Enrichment plots from the gene set enrichment analyses (GSEA).
Figure 5. Association analysis of phosphoglycerate kinase 1 (PGK1) gene expression and immune infiltration. (A) The association between PGK1 expression and 24 tumor-infiltrating lymphocytes. (B-Q) The correlation of PGK1 expression with immune infiltration level of (B) Type 2 T helper (Th2) cells, (C) T central memory (Tcm), (D) Tgd, (E) NK CD56 bright cells, (F) NK cells, (G) Type 17 T helper (Th17) cells, (H) regulatory T cells (Treg), (I) T follicular helper (TFH), (J) T effector memory (Tem), (K) dendritic cells (DC), (L) mast cells, (M) T cells, (N) cytotoxic cells, (O) CD8 T cells, (P) B cells, (Q) plasmacytoid dendritic cells (pDC).
as a molecular marker. Bioinformatics analysis was conducted to assess the prognostic value of PGK1 in HNSCC using data from TCGA. PGK1 was more highly expressed in tumor tissues compared to normal samples. In addition, PGK1 expression was an independent prognostic factor for OS in both univariate and multivariate regression analyses; high PGK1 expression was positively correlated with poor OS. High PGK1 expression has been associated with poor prognosis in breast, liver and endometrial cancer, and it may serve as a promising biomarker and target therapy for these tumors (14, 31, 32). Hence, we conjectured that PGK1 may also serve as a biomarker for HNSCC.

Figure 6. Comparison of immune cells between high- and low-phosphoglycerate kinase 1 (PGK1) expression groups. (A-P) Histogram showing the difference of Type 2 T helper (Th2) cells, T central memory (Tcm), T gamma delta (Tgd), NK CD56 bright cells, NK cells, Type 17 T helper (Th17) cells, regulatory T cells (Treg), T follicular helper (TFH), T effector memory (Tem), dendritic cells (DC), mast cells, T cells, cytotoxic cells, CD8 T cells, B cells and plasmacytoid dendritic cells (pDC) infiltration level between high- and low-PGK1 expression groups.
We found multiple oncogenes and immune-related genes were significantly associated with PGK1. The genes most positively correlated with PGK1 included P4HA1, LDHA, PDK1, NDRG1, and PFKP, while genes negatively correlated with PGK1 included TMEM125, ACKR1, COX4I2, CLEC3B, and SPNS3, some of which have been demonstrated to be related to HNSCC. For example, P4HA1, a single-gene surrogate of hypoxia, could serve as a diagnostic biomarker and independent prognostic factor in HNSCC; significant correlations have been found between the P4HA1 mRNA level and the mRNA level of several EMT and stem cell markers (33). Concerning the NDRG1, LDHA and PDK1 oncogenes, their blockage could significantly inhibit the HNSCC cell proliferation and apoptosis (34-37). To further investigate the biological function of PGK1 in HNSCC, we used TCGA data for GO, KEGG functional enrichment analysis and GSEA. The KEGG analysis showed that PGK1 influences the HNSCC development process through the adrenergic signaling in cardiomyocytes, PAR signaling pathway, dilated cardiomyopathy and primary immunodeficiency. The GSEA results showed that high PGK1 expression was mainly enriched in primary immunodeficiency, graft versus host disease, allograft rejection, asthma, and linoleic acid metabolism-related signaling pathways. There are primary immunodeficiency signaling pathways in both KEGG and GSEA results. Primary immunodeficiencies (PIDs) are genetic disorders that predispose to frequent and severe infections, autoimmunity and cancer, while the type of malignancy depends on the primary immunodeficiency, the age of the patient and possible viral infection (38). We therefore hypothesized that PGK1 was associated with immunity.

Given that tumor-infiltrating immune cells account for an indispensable component of the tumor microenvironment and that enhanced glycolytic activity in cancer is associated with pro-tumor immunity (39, 40), we sought to investigate the relationship between PGK1 and immune infiltration in HNSCC. In this study, we found that several tumor-infiltrating immune cells correlated with the expression of PGK1 in HNSCC. We further revealed a positive correlation between PGK1 expression and Th2 cells, Tcm, and Tgd. Type 2 immunity was illustrated by T helper 2 lymphocytes (Th2) and downstream cytokines (IL-4, IL-13, IL-31) as well as group 2 innate lymphoid cells (ILC2) (41). Immune cells, including T cells, are capable of mounting immune responses against tumors. The ability of the immune system to detect and eliminate neoplastic cells is known as tumor immune surveillance (42, 43). Th2 cells and type 2 immunity are involved in tumor immune surveillance, for example by reducing the size of established tumors (44). T central memory cells (Tcm), included in memory T cells show super persistence and antitumor immunity (41), and Manjarrez-Orduño found the increased frequencies of Tcm cells and enhanced tumor inflammation profiles in melanoma and non-small cell lung cancer (NSCLC) (45). These findings suggest a potential correlation between PGK1 and immune infiltration in HNSCC. However, there are some shortcomings in this study, including the need to further investigate the detailed mechanism of the impact of PGK1 on immune infiltration in HNSCC, by designing further in vivo and in vitro experiments.

Conclusion

To conclude, we demonstrate that PGK1 expression is upregulated in HNSCC and is closely associated with poor prognosis and immune cell infiltration. This study lays the foundation for a detailed study of the relationship between PGK1 and tumor-associated immune cell infiltration. Our findings suggest that PGK1 could serve as a promising independent prognostic biomarker and potential immunotherapeutic target for HNSCC. Further experimental validation is needed to elucidate the biological impact and underlying mechanism of PGK1.

Conflicts of Interest

The Authors declare that there are no conflicts of interest.
Authors’ Contributions

PW: Formal analysis, visualization, writing, QW: Conceptualization, review & editing, funding support. KW: Methodology, review & editing. YYW, YLX, ZCY: Resources, formal analysis, software.

Acknowledgements

This study was supported by the Outstanding Young Talent Project of Zunyi Medical University (17zy-002) And the Construction Project of Rural Revitalization from Guizhou Province Ministry of Education (QJJS[2022]037).

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Received July 31, 2023
Revised September 10, 2023
Accepted September 15, 2023