ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

Upregulation of PLOD2 as a Potential Biomarker Associated with Poor Prognosis and Immune Infiltration in Glioma

Yingxun Hua[1,a], Jianxin Lyu[2,b,*]

[1]*College of Laboratory Medicine and Life Sciences, Wenzhou Medical University, Wenzhou, Zhejiang, China*
[2]*Key Laboratory of Laboratory Medicine, Ministry of Education, College of Laboratory Medicine and Life Science, Wenzhou Medical University, Wenzhou, Zhejiang, 325035, China*
[a] *huayingxun925@163.com*, [b]*jxlu313@163.com*
**Corresponding author*

Abstract: *Procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2 (PLOD2), a key enzyme in collagen cross-linking, is overexpressed in various solid tumors and plays an important role in tumor invasion and metastasis. However, the potential prognostic significance of PLOD2 in glioma remains unclear. Here, we analyzed PLOD2 expression across multiple cancer types using the GEPIA2, TIMER2.0, and UALCAN databases, and confirmed that PLOD2 expression was significantly elevated in glioma tissues compared to corresponding normal tissues. Furthermore, high PLOD2 expression was associated with poor prognosis in glioma patients. Additionally, we utilized the Chinese Glioma Genome Atlas (CGGA) to investigate the association between PLOD2 and the clinicopathological and molecular characteristics of glioma patients. Our findings revealed that PLOD2 expression was positively correlated with tumor malignancy (e.g., higher WHO grade). Further analysis of the biological role of PLOD2 in glioma indicated its involvement in multiple biological processes implicated in glioma development, including immune responses, inflammatory responses, and the regulation of defense responses within the immune system. Immune infiltration analysis using the CIBERSORT database uncovered correlations between high PLOD2 expression and the infiltration of various immune cell types, as well as immune checkpoints, in glioma. In summary, this study reveals that PLOD2 is a key molecule in the malignant progression of glioma, serving not only as a potential diagnostic biomarker for GBM but also as a promising novel therapeutic target for improving glioma treatment.*

Keywords: *PLOD2, Glioma, Immune, Prognosis*

1. Introduction

Glioma represents the most common, rapidly growing, aggressive, and prognostically poor primary malignant brain tumor of the central nervous system (CNS), accounting for approximately 30% of all brain and CNS tumors and 80% of all malignant brain tumors[1-3]. According to the World Health Organization (WHO) classification system, gliomas are graded from I to IV: low-grade gliomas (LGG) encompass grades I and II, while high-grade gliomas (HGG) include grades III and IV. As WHO grade increases, tumor malignancy significantly escalates. Among these, glioblastoma multiforme (GBM) exhibits the highest malignancy and most rapid progression, constituting 50% of all glioma cases. Even with standard treatment, including maximal safe surgical resection followed by postoperative radiotherapy and chemotherapy, the 5-year survival rate remains only 5.5%, often accompanied by poor prognosis and high recurrence rates[3-5]. The core reasons for the poor prognosis of glioma include its infiltrative growth pattern, high heterogeneity, immunosuppressive microenvironment, stem cell-like properties, and frequent chemoresistance[6-8]. Therefore, a deeper understanding of the molecular characteristics of glioma and the identification of novel prognostic markers and therapeutic targets are of great significance for the diagnosis, treatment, and prognosis of glioma patients.

Collagen cross-linking and deposition depend on lysyl hydroxylation catalyzed by procollagen-lysine, 2-oxoglutarate 5-dioxygenase (PLOD)[9]. The PLOD family comprises three isoforms: PLOD1, PLOD2, and PLOD3[10]. Among these, PLOD2 is crucial for stabilizing collagen cross-link formation via hydroxylysine residues. Increased collagen deposition has been shown to promote cell adhesion, migration, growth, and survival[9]. Previous studies have demonstrated that breast cancer and lung cancer

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

with high PLOD2 expression exhibit higher migration and metastasis rates, while knocking down or inhibiting PLOD2 expression significantly suppresses cancer cell migration and invasion[11, 12]. Furthermore, PLOD2 is frequently overexpressed in various malignant tumors, including glioblastoma[12], hepatocellular carcinoma[13], pancreatic cancer[11], sarcoma[14], and renal cell carcinoma[15], and is associated with poor prognosis. These findings suggest that PLOD2 may serve as a potential anti-cancer target.

In this study, through differential gene expression enrichment analysis and immune cell infiltration analysis, we revealed significant upregulation of PLOD2 in glioma. Its expression level was significantly associated with tumor malignant progression (e.g., higher WHO grade, shorter survival) and poor patient prognosis. Collectively, our findings indicate that PLOD2 not only serves as a potential diagnostic biomarker for glioblastoma (GBM) but may also represent a novel therapeutic target for intervention.

2. Materials and Methods

2.1. Data Collection

We obtained glioma patient clinical information and RNA sequencing data from The Cancer Genome Atlas (TCGA; http://cancergenome.nih.gov/)[16] and the Chinese Glioma Genome Atlas (CGGA; http://www.cgga.org.cn/)[17] databases. Gene expression data for normal brain tissue were acquired from the Genotype-Tissue Expression (GTEx; https://xenabrowser.net/datapages/) database[18].

2.2. GEPIA2 Analysis

GEPIA2 (http://gepia2.cancer-pku.cn/) is a web tool based on data from the TCGA and GTEx databases[19]. It allows for general gene analysis, differential expression analysis, survival analysis, and correlation analysis between genes or gene sets. In this study, GEPIA2 was used to analyze the differential expression of PLOD2 mRNA in glioblastoma (GBM), lower-grade glioma (LGG), and 31 other cancer types compared to their corresponding normal tissues, and to assess the prognostic value of PLOD2 in GBM and LGG. Correlation analysis was performed between PLOD2 and related immune checkpoint molecules. Differences in transcriptional expression were compared by Student's t-test, with statistical significance defined as $p < 0.05$.

2.3. UALCAN

UALCAN (http://ualcan.path.uab.edu) is an interactive web resource based on clinical data from 31 cancer types in the TCGA database and level 3 RNA-seq data, providing graphical representations of the relative transcriptional expression of target genes between tumor and normal samples, as well as their association with clinicopathologic parameters, including patient survival information[20]. In this study, UALCAN was used to analyze the mRNA and protein expression of PLOD2 in GBM and LGG patients. Differences in transcriptional expression were compared using Student's t-test, with $p < 0.05$ considered statistically significant.

2.4. TIMER2.0

The TIMER2.0 database (http://timer.cistrome.org/) provides an efficient and reliable entry point for investigating tumor-immune interactions through multi-omics integration and algorithmic innovation[21]. In this study, we utilized this database to analyze the expression differences of PLOD2 between tumor tissues and their corresponding normal tissues.

2.5. The Human Protein Atlas (HPA)

The Human Protein Atlas (HPA) contains information on the expression profiles of human genes at the protein level in both normal and tumor tissues[22]. In this study, we utilized the HPA to compare PLOD2 protein expression between normal brain tissue and glioma tissue.

2.6. Pathological and Clinical Prognostic Analysis

We analyzed the association between PLOD2 expression and clinicopathological features in glioma patients using the CGGA database. Overall survival (OS) and disease-free survival (DFS) of glioma

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

patients with low or high PLOD2 expression in the TCGA database were analyzed using the GEPIA2 online platform. Furthermore, OS and DFS of glioma patients with low or high PLOD2 expression in the CGGA database were analyzed. The "timeROC" R package was used to plot receiver operating characteristic (ROC) curves assessing the association of PLOD2 expression with 1-year, 3-year, and 5-year survival rates.

2.7. KEGG Pathway Enrichment Analysis

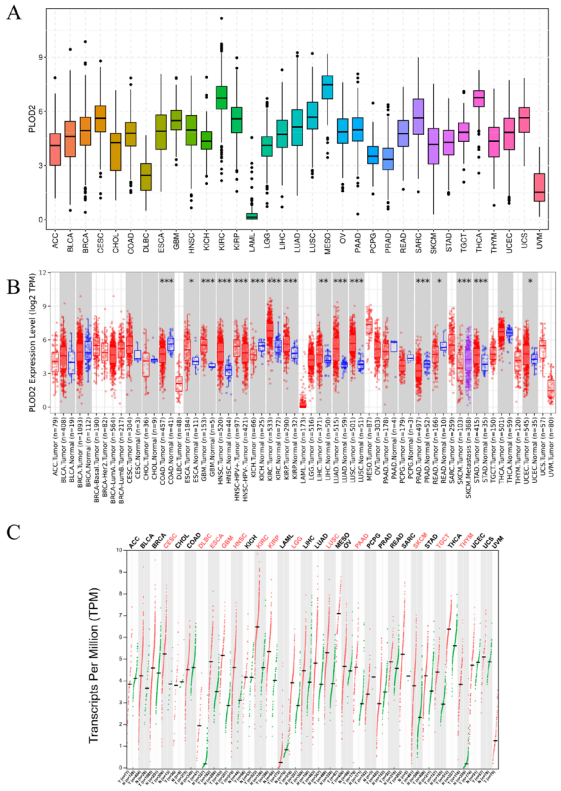
We employed the "clusterProfiler" R package to conduct Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis for PLOD2-associated differentially expressed genes.

2.8. Immune Infiltration Analysis

Infiltration data for immune cells in glioma were obtained from the CIBERSORT database (http://CIBERSORT.stanford.edu/)[23]. Differences in immune cell infiltration levels between glioma samples with high and low PLOD2 expression were assessed using the Wilcoxon rank-sum test. Spearman's correlation analysis was performed to calculate the correlation coefficients between PLOD2 expression levels and different immune cell types; a p-value < 0.05 was considered statistically significant. Subsequently, Pearson correlation analysis was applied to identify immune checkpoints significantly associated with PLOD2 expression, using a threshold of $p < 0.001$.

3. Results

3.1. Expression Pattern of PLOD2 in Pan-Cancer Perspective



*A: PLOD2 mRNA expression across pan-cancer types based on the TCGA database. B: Differential PLOD2 expression between tumor tissues and corresponding normal tissues analyzed using the TIMER2.0 online platform (*p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001). C: Differential PLOD2 mRNA expression between tumor and normal tissues analyzed by integrating TCGA and GTEx databases using the GEPIA2 online platform.*

Figure 1: Expression Pattern of PLOD2 in Pan-Cancer Analysis.

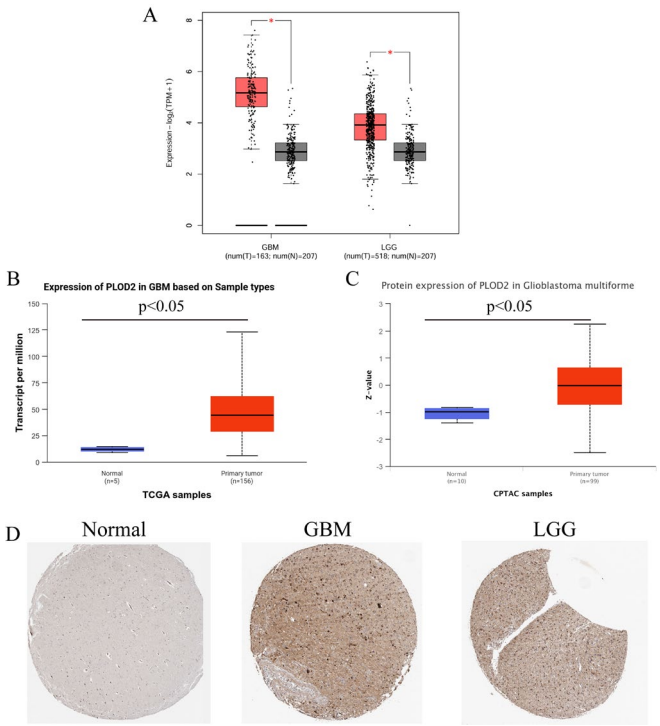
To evaluate the mRNA expression pattern of PLOD2 across cancers, we analyzed its expression levels

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

in various tumor types based on the TCGA database. The analysis results showed that PLOD2 was frequently overexpressed across a wide range of malignancies (**Fig. 1A**). Furthermore, to investigate the differential expression of PLOD2 between tumor tissues and their corresponding normal tissues, we performed analysis using the TIMER2.0 database. The results demonstrated that PLOD2 expression was generally upregulated in tumor tissues compared to corresponding normal tissues (**Fig. 1B**). To validate this finding, we integrated data from the TCGA and GTEx databases using the GEPIA2 database. This integrated analysis further confirmed significant differences in PLOD2 expression between tumor and normal tissues, with notably elevated expression levels observed in glioblastoma multiforme (GBM), head and neck squamous cell carcinoma (HNSC), lower-grade glioma (LGG), kidney renal clear cell carcinoma (KIRC), liver hepatocellular carcinoma (LIHC), lung adenocarcinoma (LUAD), and lung squamous cell carcinoma (LUSC) (**Fig. 1C**). Collectively, these data indicate aberrantly high expression of PLOD2 in multiple cancer types.

3.2. PLOD2 mRNA and Protein Expression are Upregulated in Glioma

To clarify the mRNA and protein expression levels of PLOD2 in glioma, we performed integrated analyses using the GEPIA2, UALCAN, and HPA databases. Analysis of GEPIA2 and UALCAN database results showed that PLOD2 mRNA expression levels were significantly upregulated in glioma tissues compared to adjacent normal tissues (**Fig. 2A-B**). Further analysis of protein expression using the UALCAN database indicated that PLOD2 protein expression levels were also significantly higher in glioma tissues than in adjacent normal tissues (**Fig. 2C**). Additionally, immunohistochemical staining results from the HPA database further confirmed significantly elevated PLOD2 protein expression in both glioblastoma (GBM) and lower-grade glioma (LGG) tissues **(Fig. 2D**). Collectively, these results demonstrate that both mRNA and protein expression of PLOD2 are upregulated in glioma.



*A: Differential PLOD2 mRNA expression in GBM and LGG analyzed using the GEPIA2 database (*p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001). B-C: Differential PLOD2 mRNA and protein expression in GBM analyzed using the UALCAN database. D: Representative immunohistochemical staining results of PLOD2 protein in GBM and LGG tumor tissues versus normal tissues from the HPA database.*

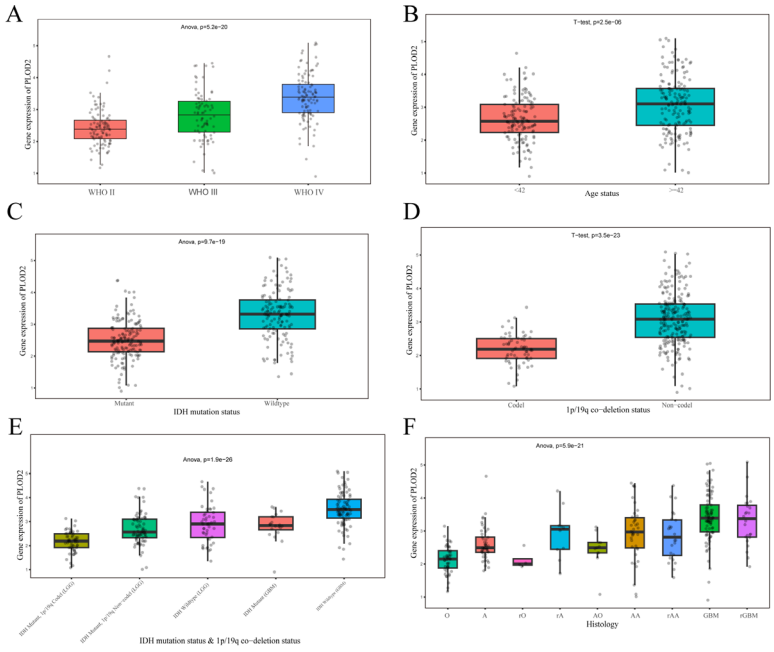
Figure 2: PLOD2 Expression in Glioma.

3.3. PLOD2 Overexpression is Significantly Associated with Glioma Clinical and Molecular Features

Given the aberrantly high expression of PLOD2 in glioma tissues, we subsequently investigated its correlation with clinical and molecular features of glioma. Analysis of PLOD2 expression across

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

different WHO grades of glioma within the CGGA database revealed a significant positive correlation between PLOD2 expression levels and WHO grade (**Fig. 3A**), with PLOD2 expression showing a clear upward trend as grade increased. Furthermore, PLOD2 expression levels also exhibited a significant positive correlation with patient age (**Fig. 3B**), suggesting its potential association with treatment resistance and poor prognosis in glioma patients. Previous studies have established that IDH mutation and 1p/19q codeletion are critical molecular events in glioma development and are closely associated with patient prognosis[23-25]. Consequently, we evaluated these molecular alteration statuses in glioma patients from the CGGA database. The analysis results showed that PLOD2 expression levels were significantly lower in the IDH-mutant group and the 1p/19q codeleted group compared to their respective wild-type groups (**Fig. 3C-E**). At the histopathological level, PLOD2 expression levels were significantly higher in recurrent glioblastoma (GBM) than in other subgroups (**Fig. 3F**). These findings suggest that PLOD2 may serve as a potential therapeutic target in glioma, with its expression level closely associated with tumor malignant progression, treatment resistance, and poor patient prognosis.



*A: Association between PLOD2 expression levels and WHO grade in glioma patients from the CGGA database. B: Association between PLOD2 expression levels and patient age in glioma patients from the CGGA database. C-E: Relationship between PLOD2 expression levels and patient genetic molecular alterations (IDH mutation, 1p/19q codeletion). (*p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001). F: Association between PLOD2 expression levels and glioma histopathology in patients from the CGGA database.*

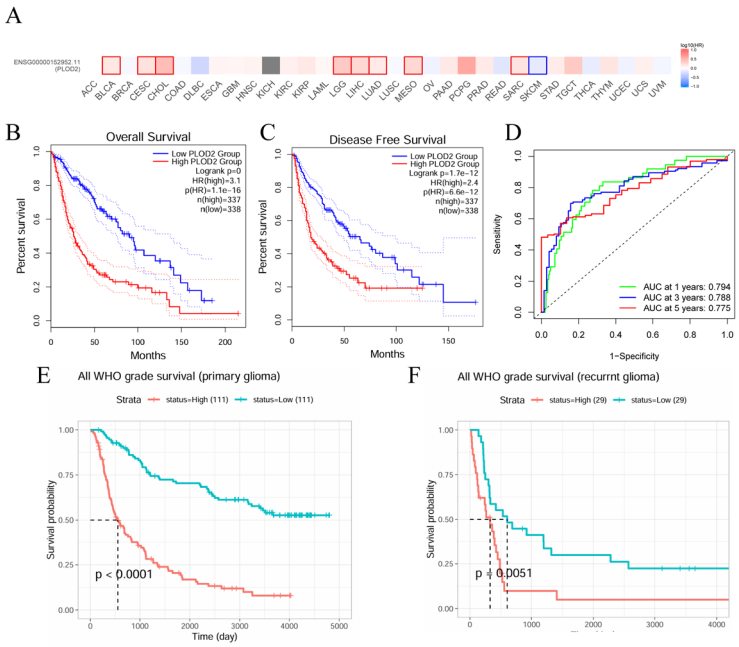
Figure 3: Relationship between PLOD2 Expression and Clinical and Genetic Molecular Features of Glioma.

3.4. Prognostic Value of PLOD2 mRNA Expression in GBM and LGG Patients

To investigate the prognostic value of PLOD2 mRNA expression, we analyzed 33 cancer types in the TCGA database based on the GEPIA2 database. Survival analysis results showed that high PLOD2 mRNA expression was associated with significantly shorter overall survival (OS) in patients with bladder urothelial carcinoma (BLCA), cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC), glioblastoma multiforme (GBM), and lower-grade glioma (LGG) (**Fig. 4A**). Focusing further on glioma, we integrated and analyzed clinical data from glioma patients in the TCGA and CGGA databases. After stratifying patients into high-expression and low-expression groups based on PLOD2 expression levels, TCGA data analysis revealed that patients in the high-expression group exhibited significantly shorter OS and disease-free survival (DFS) than those in the low-expression group **(Fig. 4B-C**). To evaluate the predictive value of PLOD2 expression levels for the prognosis of glioma patients, we constructed ROC curves for 1-year, 3-year, and 5-year survival and calculated the corresponding area under the curve (AUC) values. In the TCGA dataset, the AUC values for 1-year, 3-year, and 5-year survival all exceeded 0.7 **(Fig. 4D)**, demonstrating significant predictive accuracy. Additionally, analysis

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

of the CGGA database further confirmed that, in both primary and recurrent glioma patients, the survival time of the low PLOD2 expression group was significantly longer than that of the high-expression group (Fig. 4E-F). These results indicate that elevated PLOD2 expression is significantly associated with poor patient prognosis. In glioma, high PLOD2 expression serves as an important marker of poor prognosis, and its expression level possesses high predictive value for patient prognostic risk.



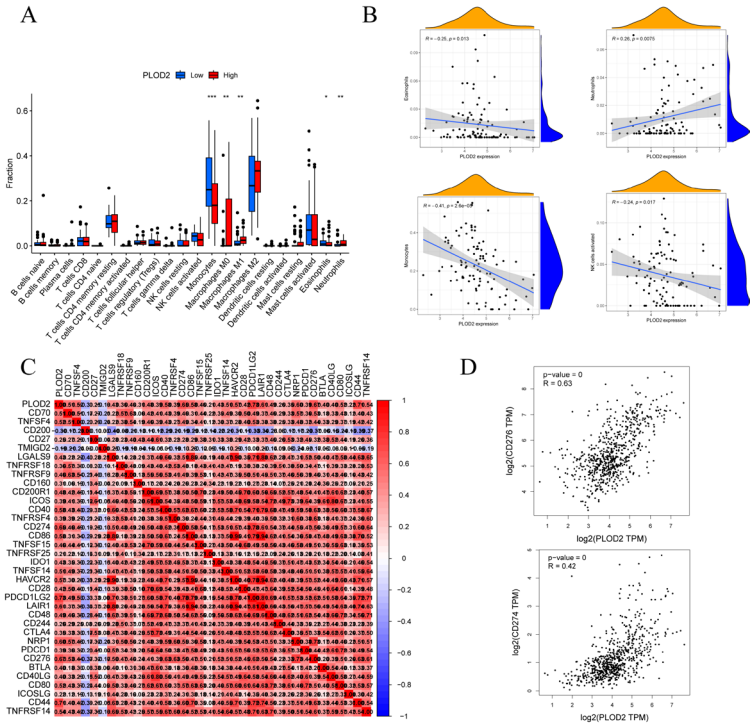
A: Prognostic value of PLOD2 mRNA expression in 33 cancer types from the TCGA database. B-D: Overall survival (OS) curves, disease-free survival (DFS) curves, and ROC curves for glioma patients with low or high PLOD2 expression based on data from the TCGA database. E-F: Correlation between PLOD2 expression levels and patient survival in primary and recurrent glioma patients from the CGGA database.

Figure 4: Prognostic Value of PLOD2 Expression in Glioma Patients.

3.5. PLOD2 Expression Correlates with Immune Cell Infiltration and Immune Checkpoint Molecules in Glioma

Given the important predictive value of immune cell infiltration within the tumor microenvironment (TME) for prognosis[26-28], we further investigated the impact of PLOD2 expression levels on tumor-infiltrating immune cells (TIICs). Based on glioma samples from the TCGA database, we analyzed the distribution differences of 22 immune cell types between the high and low PLOD2 expression groups (**Fig. 5A**). The results demonstrated that the infiltration levels of activated B cells, macrophages, regulatory T cells (Tregs), neutrophils, and CD8+ T cells were significantly positively correlated with PLOD2 expression. Conversely, the infiltration levels of activated mast cells, activated natural killer (NK) cells, and basophils were significantly negatively correlated with PLOD2 expression **(Fig. 5A-B)**. Considering the critical role of immune checkpoint molecules in regulating anti-tumor immune responses, we further analyzed the correlation between PLOD2 expression levels and the expression of immune checkpoint molecules. Correlation analysis revealed that PLOD2 expression showed significant positive correlations with immune checkpoint molecules such as PD-L1 (CD274), CD276 (B7-H3), and IDO1 (**Fig. 5C-D**). These findings reveal a potential role for PLOD2 in regulating the infiltration of specific immune cell subsets in glioma and suggest its possible influence on tumor sensitivity to immune checkpoint inhibitor therapy.

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

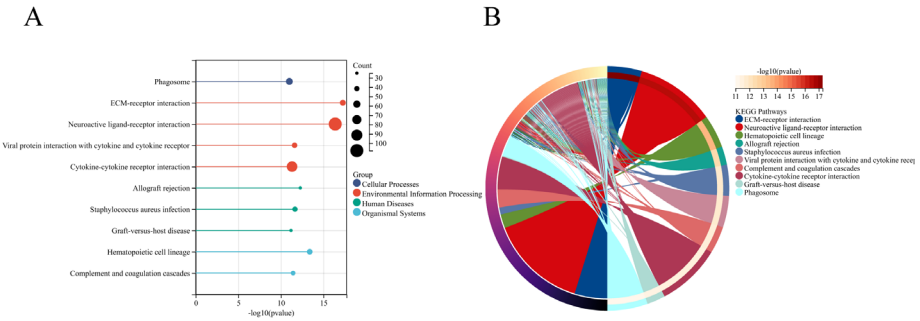


*A: Infiltration differences of 22 TIIC types between the high PLOD2 expression group and the low PLOD2 expression group. B: Correlation analysis between basophils, neutrophils, macrophages, activated NK cells, and PLOD2 expression. C: Correlation between PLOD2 and immune checkpoint genes. (Blue denotes negative correlation; red denotes positive correlation. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001). D: Correlation analysis between CD274, CD276, and PLOD2 using the GEPIA2 database.*

Figure 5: PLOD2 Expression Levels Influence Immune Cell Infiltration in Glioma.

3.6. Potential Functional Analysis of PLOD2

To further explore the potential function of PLOD2 in glioma, we stratified glioma samples from the TCGA database into high-expression and low-expression groups based on PLOD2 expression levels in tumor tissues. Subsequently, differential expression analysis between the two groups was performed using R language to identify differentially expressed genes (DEGs). To elucidate the biological processes involving these DEGs, we conducted KEGG pathway enrichment analysis for PLOD2-associated DEGs. The results indicated that these DEGs were significantly enriched in multiple biological pathways, including cytokine-cytokine receptor interaction, extracellular matrix (ECM)-receptor interaction, and neuroactive ligand-receptor interaction (**Fig. 6A-B**). These analyses provide crucial clues for further understanding the molecular mechanisms of PLOD2 in glioma.



A-B: KEGG pathway enrichment analysis of differentially expressed genes in glioma samples from the TCGA database.

Figure 6: Potential Functional Analysis of PLOD2.

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

4. Discussion

Glioma is the most common and aggressive primary malignant tumor of the central nervous system (CNS)[29, 30]. Among these, glioblastoma multiforme (GBM), as the highest grade (WHO IV) subtype, exhibits extreme malignancy and dismal patient prognosis, with a five-year survival rate of less than 10% [29, 31]. Glioma is characterized by high invasiveness and a propensity for recurrence; even after surgical resection and radiotherapy/chemotherapy, recurrence rates remain extremely high[31]. This biological behavior renders complete eradication exceedingly difficult, severely limiting treatment efficacy and ultimately leading to poor outcomes. Therefore, there is an urgent need for biomarkers or molecular signatures that can accurately predict the prognosis of glioma patients and guide individualized treatment, particularly targeted therapy and immunotherapy.

PLOD2 is a lysyl hydroxylase 2 enzyme that regulates the formation of stable cross-links in collagen. Collagen deposition is considered to play a crucial role in tumor migration, enhancing the invasion and metastasis of various cancer cell types, including breast cancer[12], hepatocellular carcinoma[13], glioma [12], and sarcoma[14]. Concurrently, in many of these cancers, clinical data indicate that increased PLOD2 expression serves as a valid and independent factor for poor prognosis and is associated with reduced survival[12]. Our study demonstrated that PLOD2 is significantly upregulated in glioma, and this high expression is significantly associated with tumor stage, molecular genetic features, and poor prognosis in glioma patients. Tumor immune escape represents a critical mechanism by which tumors evade host immune surveillance[32]. We further explored the immunomodulatory function of PLOD2 in glioma and found that PLOD2 is involved in multiple immune response processes and shows significant correlations with immune cell infiltration and immune checkpoint expression in glioma.

Nevertheless, our study has certain limitations. First, the analysis of PLOD2 expression and its prognostic impact was conducted using online public databases; further studies with clinical samples are needed to validate these results. Second, to further investigate the detailed mechanisms underlying the effects of PLOD2 on glioma, both in vitro and in vivo experiments should be designed for verification.

5. Conclusions

In conclusion, our study demonstrates that PLOD2 mRNA and protein expression are upregulated in glioma, and high PLOD2 expression is associated with poor prognosis in glioma patients. Therefore, PLOD2 may serve as a potential biomarker for poor prognosis and may play a specific role in immune infiltration in glioma.

References

[1] Jackson CM, Choi J, Lim M. Mechanisms of immunotherapy resistance: lessons from glioblastoma. Nat Immunol[J]. 2019,20(9):1100-1109.
[2] You H, Geng S, Li S, et al. Recent advances in biomimetic strategies for the immunotherapy of glioblastoma. Biomaterials[J]. 2024,311:122694.
[3] Chen R, Smith-Cohn M, Cohen AL, et al. Glioma Subclassifications and Their Clinical Significance. Neurotherapeutics[J]. 2017,14(2):284-297.
[4] Weller M, Wen PY, Chang SM, et al. Glioma. Nat Rev Dis Primers[J]. 2024,10(1):33.
[5] Thakkar JP, Dolecek TA, Horbinski C, et al. Epidemiologic and molecular prognostic review of glioblastoma. Cancer Epidemiol Biomarkers Prev[J]. 2014,23(10):1985-1996.
[6] Sottoriva A, Spiteri I, Piccirillo SG, et al. Intratumor heterogeneity in human glioblastoma reflects cancer evolutionary dynamics. Proc Natl Acad Sci U S A[J]. 2013,110(10):4009-4014.
[7] Osswald M, Jung E, Sahm F, et al. Brain tumour cells interconnect to a functional and resistant network. Nature[J]. 2015,528(7580):93-98.
[8] Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol[J]. 2021,23(8):1231-1251.
[9] Wells RG. The role of matrix stiffness in regulating cell behavior. Hepatology[J]. 2008,47(4):1394-1400.
[10] van der Slot AJ, Zuurmond AM, Bardoel AF, et al. Identification of PLOD2 as telopeptide lysyl hydroxylase, an important enzyme in fibrosis. J Biol Chem[J]. 2003,278(42):40967-40972.
[11] Sada M, Ohuchida K, Horioka K, et al. Hypoxic stellate cells of pancreatic cancer stroma regulate extracellular matrix fiber organization and cancer cell motility. Cancer Lett[J]. 2016,372(2):210-218.
[12] Du H, Pang M, Hou X, et al. PLOD2 in cancer research. Biomed Pharmacother[J]. 2017,90:670-

ISSN 2618-1584 Vol. 8, Issue 2: 35-43, DOI: 10.25236/FMSR.2026.080205

676.
[13] Noda T, Yamamoto H, Takemasa I, et al. PLOD2 induced under hypoxia is a novel prognostic factor for hepatocellular carcinoma after curative resection. Liver Int[J]. 2012,32(1):110-118.
[14] Eisinger-Mathason TS, Zhang M, Qiu Q, et al. Hypoxia-dependent modification of collagen networks promotes sarcoma metastasis. Cancer Discov[J]. 2013,3(10):1190-1205.
[15] Kurozumi A, Kato M, Goto Y, et al. Regulation of the collagen cross-linking enzymes LOXL2 and PLOD2 by tumor-suppressive microRNA-26a/b in renal cell carcinoma. Int J Oncol[J]. 2016, 48(5):1837-1846.
[16] Tomczak K, Czerwińska P, Wiznerowicz M. The Cancer Genome Atlas (TCGA): an immeasurable source of knowledge. Contemp Oncol (Pozn)[J]. 2015,19(1a):A68-A77.
[17] Zhao Z, Zhang KN, Wang Q, et al. Chinese Glioma Genome Atlas (CGGA): A Comprehensive Resource with Functional Genomic Data from Chinese Glioma Patients. Genomics Proteomics Bioinformatics[J]. 2021,19(1):1-12.
[18] Carithers LJ, Moore HM. The Genotype-Tissue Expression (GTEx) Project. Biopreserv Biobank[J]. 2015,13(5):307-308.
[19] Tang Z, Kang B, Li C, et al. GEPIA2: an enhanced web server for large-scale expression profiling and interactive analysis. Nucleic Acids Res[J]. 2019,47(W1):W556-w560.
[20] Chandrashekar DS, Bashel B, Balasubramanya SAH, et al. UALCAN: A Portal for Facilitating Tumor Subgroup Gene Expression and Survival Analyses. Neoplasia[J]. 2017,19(8):649-658.
[21] Li T, Fu J, Zeng Z, et al. TIMER2.0 for analysis of tumor-infiltrating immune cells. Nucleic Acids Res[J]. 2020,48(W1):W509-w14.
[22] Thul PJ, Lindskog C. The human protein atlas: A spatial map of the human proteome. Protein Sci[J]. 2018,27(1):233-244.
[23] Chen B, Khodadoust MS, Liu CL, et al. Profiling Tumor Infiltrating Immune Cells with CIBERSORT. Methods Mol Biol[J]. 2018,1711:243-59.
[24] Murugan AK, Alzahrani AS. Isocitrate Dehydrogenase IDH1 and IDH2 Mutations in Human Cancer: Prognostic Implications for Gliomas. Br J Biomed Sci[J]. 2022,79:10208.
[25] Figarella-Branger D, Colin C, Mokhtari K, et al. Reappraisal of prognostic factors in CNS WHO grade 3 oligodendrogliomas IDH-mutant and 1p/19q co-deleted: Lessons from the French POLA cohort. Neuro Oncol[J]. 2025,27(3):755-766.
[26] Fridman WH, Zitvogel L, Sautès-Fridman C, et al. The immune contexture in cancer prognosis and treatment. Nat Rev Clin Oncol[J]. 2017,14(12):717-734.
[27] Quail DF, Joyce JA. The Microenvironmental Landscape of Brain Tumors. Cancer Cell[J]. 2017,31(3):326-341.
[28] Newman AM, Liu CL, Green MR, et al. Robust enumeration of cell subsets from tissue expression profiles. Nat Methods[J]. 2015,12(5):453-457.
[29] Ostrom QT, Patil N, Cioffi G, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2013-2017. Neuro Oncol[J]. 2020,22(12 Suppl 2):iv1-iv96.
[30] Weller M, van den Bent M, Preusser M, et al. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. Nat Rev Clin Oncol[J]. 2021,18(3):170-186.
[31] Juratli TA, Schackert G, Krex D. Current status of local therapy in malignant gliomas--a clinical review of three selected approaches. Pharmacol Ther[J]. 2013,139(3):341-358.
[32] Huang B, Zhang J, Zong W, et al. Myeloidcells in the immunosuppressive microenvironment in glioblastoma: The characteristics and therapeutic strategies. Front Immunol[J]. 2023,14:994698.