Original Article

Screening of potential key pathogenic and intervention targets of low-grade glioma based on bioinformatics

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Background: Sialic acid-binding immunoglobulin-like lectin 8 (*SIGLEC8*) is involved in the progression of numerous diseases. This study aimed to examine the relationship between *SIGLEC8* and the prognosis of patients with low-grade glioma (LGG) and the related mechanisms.

Methods: First, screening of the differentially expressed genes (DEGs) *SIGLEC8* in The Cancer Genome Atlas (TCGA) database was performed. The expression was then correlated with the prognosis of patients with LGG and then verified using the Tumor Immune Estimation Resource (TIMER) and TCGA databases. Cox regression was employed to conduct multifactorial analysis and was followed by the construction of an internally validated nomogram based on these results. To investigate the possible mechanisms, we used gene set enrichment analysis (GSEA). We conducted a retrospective analysis of the clinical information of patients with LGG who were treated at Longgang Central Hospital of Shenzhen from January 2018 to December 2020 and from whom tumor and peritumoral tissues were taken during surgery. Expression of essential genes was identified by employing quantitative real-time polymerase chain reaction (qRT-PCR). Multivariate analysis, via Cox regression, was employed to determine the prognostic factors for patients with LGG.

Results: The transcriptional activity of *SIGLEC8* was found to be elevated in LGG neoplastic tissues compared to neighboring nonneoplastic tissues. Overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) were improved in patients with LGG with reduced expression of *SIGLEC8* as compared to those with increased expression of *SIGLEC8*. The nomogram's C-index is 0.804 (0.781–0.827). indicating good predictive accuracy. GSEA revealed that *SIGLEC8* might influence LGG biological events by participating in the PD-1, IL3, JAK/STAT, and PI3KCI signal transduction pathways, as well as cytokine and inflammatory response, cell cycle, homeostasis, and extracellular matrix. This study included 72 patients with LGG. qRT-PCR showed upregulated *SIGLEC8* expression in LGG tumor tissues, which was significantly associated with tumor number and metastasis to the lymph nodes ($P<0.05$). Multivariate analysis using Cox regression identified the high expression of *SIGLEC8* as an independent risk factor in LGG prognosis ($P<0.05$).

Conclusions: For the prognosis of patients with LGG, the transcriptional activity of *SIGLEC8* is increased in LGG tissues and is an independent risk factor. Interference with *SIGLEC8* could promote tumor progression by regulating the JAK/STAT signaling pathway, indicating that *SIGLEC8* may function as a distinctive predictive biomarker for patients with LGG.

Keywords: *SIGLEC8*; low-grade glioma (LGG); prognosis; bioinformatics; independent risk factor

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Introduction

Gliomas are common tumors of the brain and spinal cord in the central nervous system. Among all primary central nervous system malignant tumors, 80.8% are gliomas. Low-grade gliomas (LGGs) are one of the prevalent types of gliomas, constituting 16% of all gliomas (1,2). Compared to high-grade gliomas (such as glioblastoma), the prognosis of LGG is better, yet approximately 70% of LGG cases progress within 10 years (3). LGG is highly invasive, rendering complete cure difficult, and the absence of reliable prognostic indicators for evaluating tumor prognosis is a significant challenge. The tumor microenvironment, composed of various stromal cells, some nontumor components, and immune cells, plays a crucial role in tumorigenesis and progression (4). Therefore, identifying effective therapeutic targets and predictive biomarkers is critical to improving treatment.

Sialic acid is an essential part of the glycoproteins and glycolipids found in the cell membrane and is recognized by activated T cells and a series of surface proteins present in innate immune cells (5,6). Typically, the serum levels of sialic acid content in the human body are stable. However, in malignant tumors, elevated serum levels of sialic acid can be found. The sialic acid released in the blood might be shed from the cancer cell surface due to significant modifications in the content and structure of glycoproteins and glycolipids found on the cancerous cell membrane (7). Therefore, serum sialic acid is an important clinical marker for tumor diagnosis. Receptors that recognize sialylated glycans are called sialic acid-binding immunoglobulin-like lectins (Siglecs). They belong to the immunoglobulin superfamily (IgSF) and are a newly discovered family of type I transmembrane proteins (8). Commonly expressed in innate and adaptive immune cells, *SIGLEC8* exerts crucial functions in immune cell signaling. Each member of the Siglec family has a unique expression pattern, with *SIGLEC8* predominantly acting on eosinophils (9). Currently, research on *SIGLEC8* in tumors is limited, and there are no studies on *SIGLEC8* in LGG.

Our study's primary aim was to examine the transcriptional activity of *SIGLEC8* and its role in the prognosis of patients with LGG. A retrospective analysis of the clinical information of patients with LGG who had undergone treatment at Longgang Central Hospital of Shenzhen was conducted. By using quantitative real-time polymerase chain reaction (qRT-PCR) to detect the expression of key genes in LGG tumor tissues and analyzing the correlation between key gene expression and prognosis of LGG patients, the clinical value of key genes can be further clarified. We present this article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1662/rc).

Highlight box

Key findings

- Sialic acid-binding immunoglobulin-like lectin 8 (*SIGLEC8*) transcriptional activity is significantly elevated in low-grade glioma (LGG) tissues compared to nonneoplastic tissues. High *SIGLEC8* expression is an independent risk factor for poor prognosis in patients with LGG. *SIGLEC8* influences LGG biological events via the PD-1, IL3, JAK/STAT, and PI3KCI signaling pathways, as well as cytokine response, cell cycle, homeostasis, and extracellular matrix.

What is known and what is new?

- SIGLEC8 is involved in the progression of various diseases.
- This study identified *SIGLEC8* to be a significant prognostic marker in LGG, demonstrating its elevated expression in LGG tissues and its association with poorer patient outcomes.

What is the implication, and what should change now?

- *SIGLEC8*'s role in LGG supports its potential as a target for therapeutic intervention.
- Further research should explore targeted therapies aimed at modulating *SIGLEC8* activity to improve the prognosis and survival rates of patients with LGG.

Methods

Data analysis using the Tumor Immune Estimation Resource (TIMER) and The Cancer Genome Atlas (TCGA) databases

The expression data of Sialic acid-binding immunoglobulin-like lectin 8 (SIGLEC8) across different cancer types were extracted from the TIMER database. Using the TIMER database, *SIGLEC8* expression data were screened from

LGG cancer tissue and normal brain tissue. Simultaneously, to validate the results obtained from the TIMER database and to gather more comprehensive information, we also downloaded RNA-seq data related to LGG from the TCGA database. After obtaining the data, bioinformatics methods were employed to process and analyze the data, ensuring quality control and preprocessing for accuracy and consistency. Statistical methods were then applied to compare the expression levels of *SIGLEC8* in LGG cancer tissues and normal tissues, aiming to reveal its potential biological significance.

Clinical parameters of patients with LGG in TCGA database and their relationship with SIGLEC8

To further investigate the potential clinical significance of *SIGLEC8* in LGG, we systematically obtained a comprehensive clinical dataset of LGG patients from TCGA database. Spearman rank correlation analysis and Cox proportional hazards regression model were employed to rigorously evaluate the association between *SIGLEC8* expression and patient survival time.

Nomogram construction and evaluation

Based on the results of multivariate analysis, we constructed a nomogram to visually represent the relationship between key variables and research objectives. The model was fitted using statistical software, incorporating the weights of the influencing factors identified in the multivariate regression. To assess the predictive accuracy of the nomogram, we utilized calibration curves, which compare predicted probabilities with observed outcomes. Calibration statistics, including the Hosmer-Lemeshow test, were calculated to quantitatively evaluate the nomogram's performance.

Gene set enrichment analysis (GSEA)

To better understand the functions and regulatory mechanisms of differentially expressed genes (DEGs), we used GSEA with the Metascape platform and CHDTEPDB tool (10). Prior to GSEA, we rigorously screened DEGs showing significant expression changes between the experimental and control groups. These genes were then uploaded to Metascape for comprehensive enrichment analysis. The platform provided detailed insights, including the enrichment significance of gene sets, pathway annotations, and visualized charts, highlighting key biological processes and regulatory interactions of the DEGs.

General characteristics of patients included in the study

From January 2018 to December 2020, we selected 72 patients with LGG treated at the Longgang Central Hospital of Shenzhen, including 31 females and 41 males. The age range was 36–77 years, and the mean age was 58.48±8.34 years. Among these patients, 42 had tumors located in the frontal region, whereas 30 had tumors located in the temporal region. The number of cases with a single tumor was 51, while that of multiple tumors was 21. In 27 cases, the diameter of the tumor was ≥3 cm, while 45 cases had a diameter of <3 cm. There were 23 cases of lymph node metastasis. In the classification of tumors of the central nervous system as per the World Health Organization (WHO), 34 cases were grade II, and 38 cases were grade III.

The criteria for inclusion were as follows: (I) LGG confirmed by pathology, computed tomography, or magnetic resonance imaging examination, (II) a first diagnosis of LGG, and (III) complete clinical data. Meanwhile, the criteria for exclusion were as follows: (I) age younger than 18 years; (II) presence of other brain diseases; (III) complicated with acute or chronic infections; (IV) presence of other malignant tumors or immune or hematological system disorders; (V) incomplete medical records, unwillingness to follow-up, or in-hospital death; and (VI) tumors already metastasized to other sites. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Longgang Central Hospital of Shenzhen (No. 2023ECPJ103) and informed consent was taken from all the patients or their families.

qRT-PCR

During surgery, we collected tumor tissues and peritumoral tissues (present at a distance greater than 3 cm away from the cancer tissue and confirmed histopathologically as healthy tissue) from patients with LGG. Through use of TRIzol reagent (cat No. 15596026; Thermo Fisher Scientific, Waltham, MA, USA), total cellular RNA was extracted after the tissue specimens were ground in liquid nitrogen. The TaKaRa RNA PCR Kit (cat No. RR036A; Takara Bio, Kusatsu, Japan) was used to synthesize competent DNA (cDNA). The reverse transcription system included 1 µL of PrimeScript RT Enzyme Mix (Takara

Bio), 9 µL of total RNA, and 2 µL of 5× PrimeScript Buffer (Takara Bio). The reaction proceeded for 15 minutes at 37 ℃ and for 5 seconds at 85 ℃. The SYBR Premix Ex Taq™ Kit (cat No. P505; Nanjing Novizan Biotechnology Co., Ltd., China) was used for qRT-PCR amplification. The 20-µL reaction mix contained the following: 1 µL of cDNA, 0.5 µL of each downstream and upstream primer, 0.5 µL of universal microRNA qPCR primer, 10 µL of 2× TransStart Top Green qPCR SuperMix (cat No. abx098033; Abbexa, Cambridge, UK), and 7.5 µL of nuclease-free water. The reaction was carried out at 95 ℃ for a duration of 90 seconds (1 cycle), 95 ℃ for a duration of 30 seconds, 63 ℃ for a duration of 30 seconds, and 72 ℃ for a duration of 15 seconds (40 cycles). To calculate the relative expression level of *SIGLEC8* in tissues, the $2^{-\Delta\Delta CT}$ method was employed (11). GAPDH, was used as the internal control in the experiment. The primers were as follows: *SIGLEC8* (F) 5'-CAA TAT GGG GAT GGT TAC TTGCT-3' and (R) 5'-GGA GCG TCT TGG TAT GGT CTG-3'; and GAPDH (F) 5'-GCA CCG TCA AGG CTG AGAAC-3' and (R) 5'-GGA TCT CGC TCC TGG AAG ATG-3'.

Follow-up of patients

Patients diagnosed with LGG were monitored for 3 years after discharge via telephone communication or outpatient visits. Within the first year, follow-ups were undertaken every 3 months and then every 6 months. The endpoint for follow-ups was either patient progression or the completion of the follow-up period. The 3-year progression-free survival (PFS) was recorded.

Statistical analysis

R software version 3.6.3 (The R Foundation for Statistical Computing) was employed to perform visualization and statistical analysis. To investigate the potential cellular mechanisms of *SIGLEC8*, GSEA was conducted. Data were statistically analyzed with SPSS 26.0 software (IBM Corp., Armonk, NY, USA). The measurement data, which adhered to a normal distribution, were expressed as the mean value ± standard deviation. The independent samples *t*-test was applied to compare the groups. Count data were expressed as counts and percentages and were compared between groups using the χ^2 test or Fisher exact probability test. The Kaplan-Meier method was used to evaluate patient survival, and the log-rank test was used for significance testing. Multivariate Cox regression analysis was employed to identify factors associated with the prognosis of patients with LGG. A P value less than 0.05 or a log-rank P value less than 0.05 was considered statistically significant.

Results

Transcriptional activity of SIGLEC8 in LGG and its correlation with the prognosis of patients in the TIMER and TCGA databases

According to our analysis of the TIMER database, the expression of *SIGLEC8* varies across different tumor types. For instance, *SIGLEC8* expression was significantly upregulated in BRCA, CHOL, HNSC-HPVpos, KICH, KIRC, KIRP, and THCA tissues, while it was significantly downregulated in BLCA, COAD, LIHC, LUAD, LUSC, READ, and UCEC tissues (P<0.05) (*Figure 1A*). Additionally, in both the nonpaired and paired tumor tissues of LGG, expression of *SIGLEC8* was higher as compared to adjacent nontumor tissues (*Figure 1B*). Receiver operating characteristic curve analysis indicated an area under the curve of 0.933, indicating that *SIGLEC8* has excellent predictive value (*Figure 1C*). Furthermore, after examination of the clinical data of LGG in TCGA database, we found that patients of LGG with low *SIGLEC8* expression had a better progression-free interval (PFI), overall survival (OS), and disease-specific survival (DSS) compared to those with high *SIGLEC8* expression (*Figure 1D*).

Nomogram construction

A nomogram was drawn to personalize the prediction of survival rates for 1, 3, and 5 years in patients diagnosed with LGG based on the results of multivariable analysis from TCGA database. The nomogram's C-index was 0.804 (0.781–0.827) (*Figure 2A*). Additionally, the calibration curve demonstrated that the nomogram had excellent predictive value (*Figure 2B*).

Prediction of signaling pathways based on GSEA

GSEA functional analysis was performed using Metascape online. We found that *SIGLEC8* could potentially influence LGG biological events by participating in the PD-1, IL3, PI3KCI, and JAK/STAT signal transduction pathways, as well as cytokine and inflammatory response, cell cycle, homeostasis, and extracellular matrix. These effects could

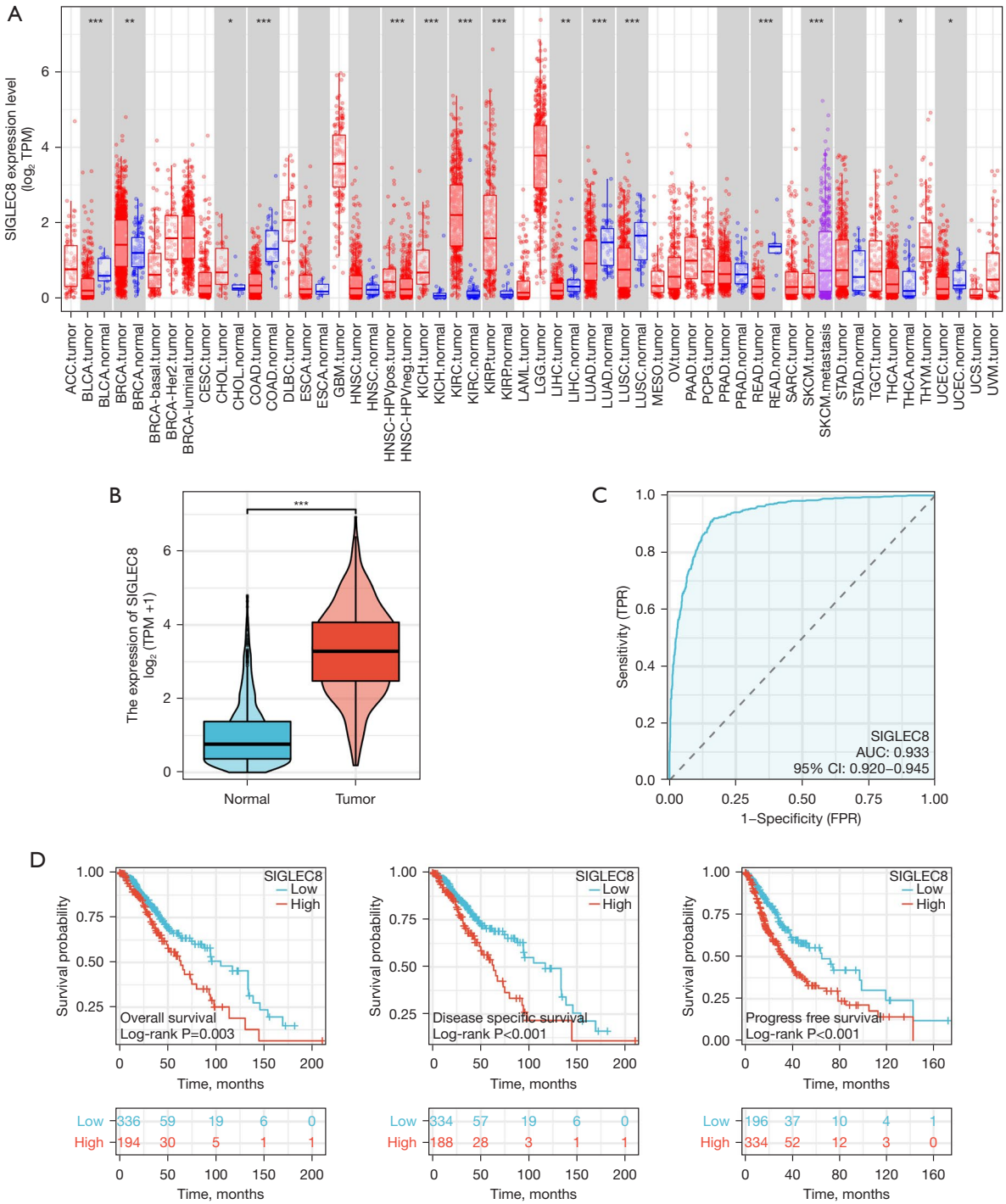

Figure 1 Expression of *SIGLEC8* in LGG and its correlation with the prognosis of patients with LGG. (A) Expression levels of *SIGLEC8* across various cancers in the TIMER database. Red represents tumor tissue, blue represents normal tissue, and purple represents distant metastatic tissue. (B) Expression levels of *SIGLEC8* in nonpaired LGG tumor tissues (n=523) and neighboring nontumor tissues (n=1,152) in TCGA database. (C) ROC curve indicating that *SIGLEC8* has a good discriminative ability between tumors and normal tissues. (D) Correlation of *SIGLEC8* expression with the prognosis of patients with LGG in TCGA database. *, P<0.05; **, P<0.01; ***, P<0.001. LGG, low-grade glioma; TPM, transcripts per million; TPR, true positive rate; FPR, false positive rate; TIMER, Tumor Immune Estimation Resource; TCGA, The Cancer Genome Atlas; ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.

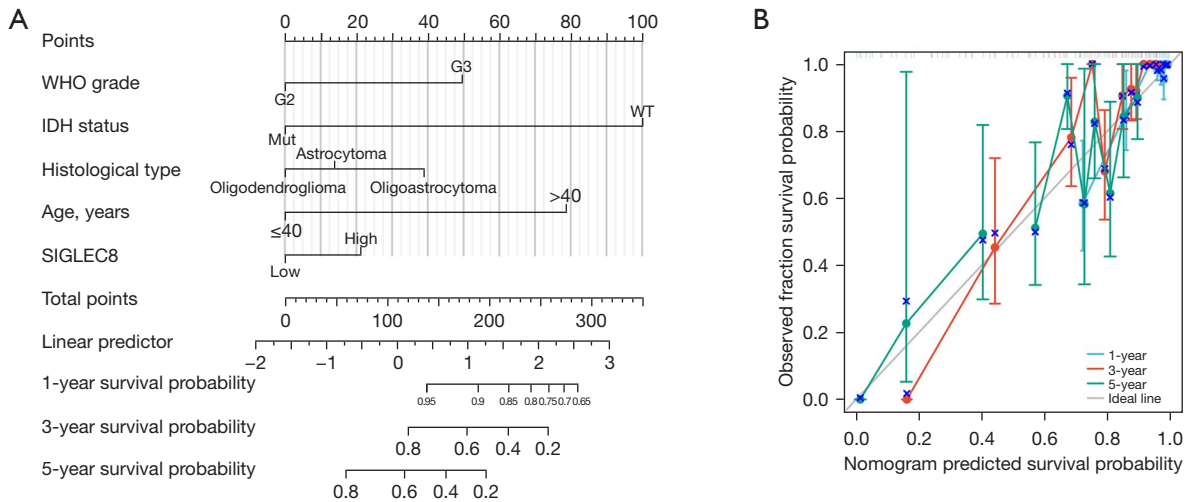

Figure 2 Nomogram and calibration plot for patients with LGG. (A) Nomogram for predicting the survival rates at 1, 3, and 5 years in patients diagnosed with LGG. (B) Calibration plot for the nomogram predicting the probability of overall survival. LGG, low-grade glioma; WHO, World Health Organization; IDH, isocitrate dehydrogenase; Mut, mutant; WT, wild type.

account for the varied prognoses in LGG (*Figure 3*).

Comparison of SIGLEC8 expression between LGG tumor tissue and neighboring healthy tissue

Results of qRT-PCR showed that the levels of transcriptional activity of *SIGLEC8* in LGG tumor tissues were substantially greater than those in neighboring healthy tissues (P<0.05) (*Table 1*).

Relationship between SIGLEC8 messenger RNA (mRNA) expression and clinicopathological characteristics of patients with LGG

The mRNA expression of *SIGLEC8* was found to be significantly correlated with the number of tumors and metastasis to lymph nodes in patients with LGG (P<0.05). However, no significant association was found for tumor location, age, sex, tumor diameter, or WHO grade (P>0.05), as detailed in *Table 2*.

Correlation between SIGLEC8 expression and the prognosis of patients with LGG

On the basis of the median *SIGLEC8* expression in LGG tissues, patients were categorized into low and high expression groups. The PFS during the follow-up period was recorded, and the PFS curve was plotted (*Figure 4*). According to the results, the mean PFS of the *SIGLEC8*–low expression group was 31.81±1.43 months (95% CI: 29.00–34.62), while the mean PFS of the *SIGLEC8*-high expression group was 26.94±1.74 months (95% CI: 23.53–30.36). The PFS of the *SIGLEC8*-high expression group was significantly shorter than that of the *SIGLEC8*-low expression group (P=0.03).

Multivariate and univariate Cox regression analysis of patients with LGG

Gender, age, number of tumors, tumor location, tumor diameter, metastatic lymph node, and WHO grade were used as independent variables; survival status was used as the dependent variable, and follow-up time was used as the time variable. Multivariate Cox regression analysis showed that multiple tumors, metastatic lymph nodes, and increased expression *SIGLEC8* were independent risk factors for mortality in patients with LGG, with the differences being statistically significant (P<0.05) (*Table 3*).

Discussion

LGG is a prevalent primary intracranial neoplasm, exhibiting significant intrinsic heterogeneity in biological behavior (12). Presently, the conventional therapy for LGG involves surgical excision in combination with postoperative radiation and chemotherapy (13). Although certain

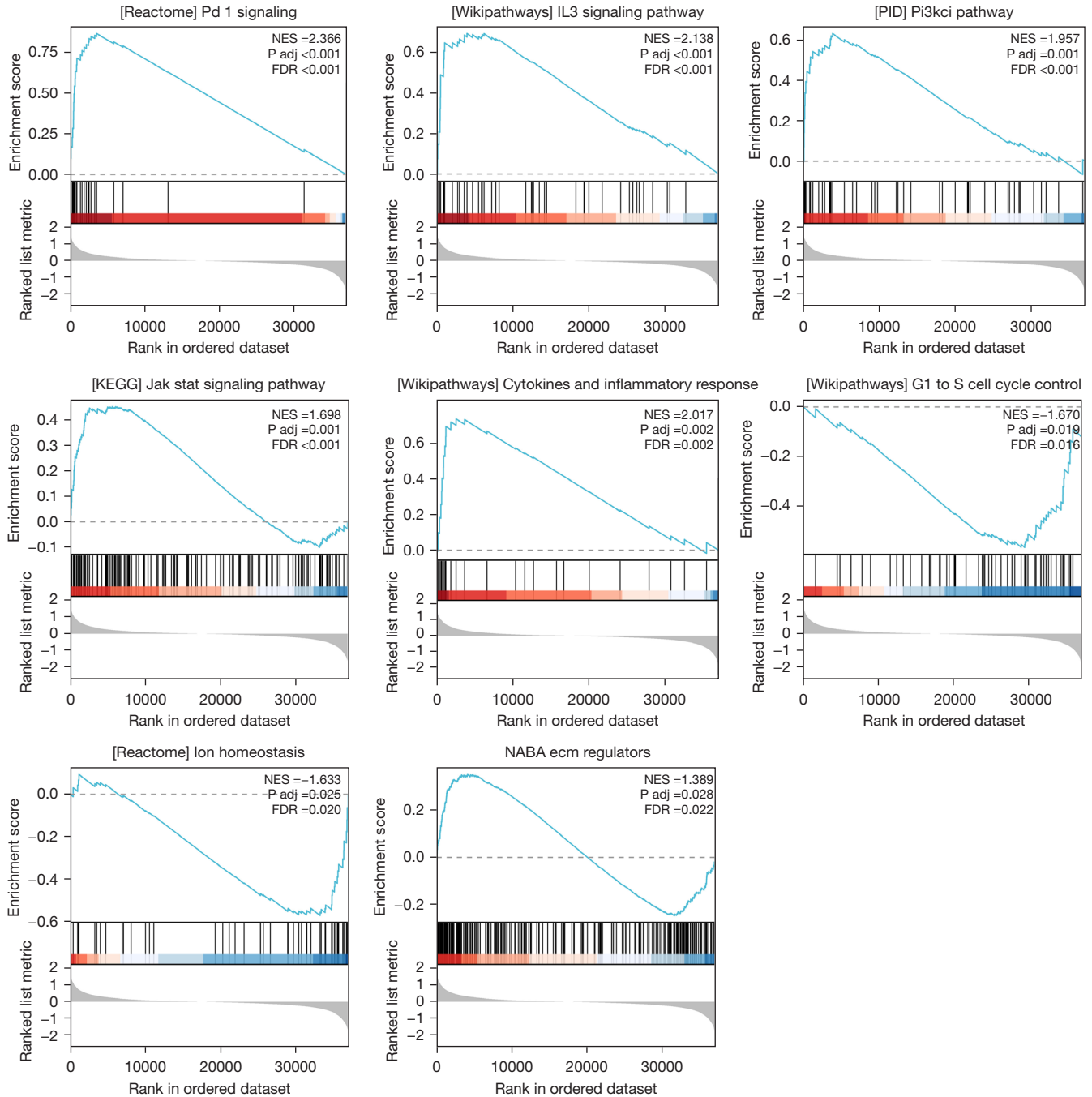

Figure 3 Statistically significant pathways in the gene set enrichment analysis. The gene sets from the MSigDB collection for biological processes were used. A total of 1,600 random sample permutations were performed. FDR, false discovery rate; NES, normalized enrichment score.

Table 1 Comparison of *SIGLEC8* expression in LGG tumor tissues and neighboring nontumor tissues

Tissue type	n	*SIGLEC8* expression ($\bar{x}$±s)	t	P
Tumor tissue	72	1.30±0.19	13.36	<0.001
Adjacent nontumor tissue	72	0.99±0.03		

LGG, low-grade glioma.

Table 2 Association between the messenger RNA expression of *SIGLEC8* and the clinicopathological characteristics of patients with LGG

Clinicopathological parameter	n	*SIGLEC8* mRNA expression ($\bar{x}$±s)	t	P
Sex			0.9384	0.35
Male	41	1.32±0.19		
Female	31	1.27±0.19		
Age (years)			1.605	0.11
<60	38	1.26±0.20		
≥60	34	1.33±0.19		
Tumor number			2.081	0.041
Single	51	1.27±0.19		
Multiple	21	1.37±0.20		
Tumor location			0.1063	0.92
Frontal	42	1.30±0.17		
Temporal	30	1.29±0.23		
Tumor diameter (cm)			1.781	0.08
≥3	27	1.35±0.21		
<3	45	1.27±0.18		
Lymph node metastasis			2.247	0.03
Yes	23	1.37±0.23		
No	49	1.26±0.17		
WHO grade			1.572	0.12
II	34	1.26±0.19		
III	38	1.33±0.19		

LGG, low-grade glioma; WHO, World Health Organization.

progress has been made, issues such as tumor resistance and recurrence remain, with some LGGs progressing to high-grade gliomas (14). Therefore, elucidating the mechanisms underlying LGG development is crucial for identifying effective therapeutic targets and predictive biomarkers and for devising new treatment strategies.

In recent years, significant progress has been made in the research of LGG biomarkers, providing new perspectives on prognosis evaluation, treatment decision-making, and personalized treatment. Potential biomarkers such as EMILIN2 have been identified, with their expression and methylation status closely related to the prognosis of LGG patients. High expression or low methylation may indicate poor overall survival (15). Similarly, the methylation status of MGMT promoter and IDH mutations serve as key prognostic indicators, significantly

influencing patient outcomes and potentially affecting their response to therapy (16). As research continues to advance, personalized treatment strategies based on these biomarkers are becoming increasingly feasible. Additionally, the integration of biomarkers into prognostic assessments shows great promise, enabling healthcare providers to more accurately evaluate prognostic risks. However, due to the heterogeneity and complexity of LGG, future research should focus on discovering new biomarkers. Identifying additional biomarkers is crucial for gaining a more comprehensive understanding of LGG biology, improving prognostic accuracy, and developing more effective individualized treatment strategies.

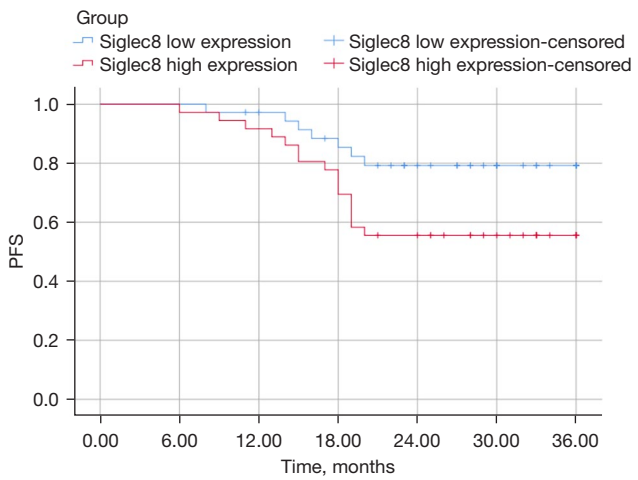

Figure 4 Association between the expression of *SIGLEC8* and the prognosis of patients with LGG. LGG, low-grade glioma; PFS, progression-free survival.

Recently, the advancement of technology in sequencing and omics has facilitated a greater understanding of the mechanisms in LGG and the pursuit of diagnostic and therapeutic objectives (17). In this study, we evaluated the role of *SIGLEC8* in the emergence of LGG and the related mechanisms by combining *in vitro* experiments with bioinformatics analytical tools. In the TCGA database, we found that *SIGLEC8* is upregulated in LGG and LGG patients with lower expression of *SIGLEC8* have improved DSS, PFI, and OS compared to those with high *SIGLEC8* expression. This suggests that *SIGLEC8* may be a crucial marker for the progression of LGG, with its high expression correlating with poorer prognosis. The nomogram constructed based on multivariable analysis results further enhanced the clinical reference value of our study molecule.

Additionally, GSEA revealed that *SIGLEC8* might influence LGG biological events by participating in the PD-1, IL3, PI3KCI, and JAK/STAT signal transduction pathways, as well as cytokine and inflammatory responses, cell cycle, homeostasis, and extracellular matrix. These pathways serve essential functions in tumor immune evasion, cell multiplication, differentiation, metabolic regulation, and the stability of the tumor microenvironment. A previous study has also explored related mechanisms. For instance, DDOST was found to mediate the immunosuppressive microenvironment of gliomas, and MELK was identified as an independent indicator for prognosis and a prospective candidate for immunotherapy for gliomas (18). Other research has found that INPP4B can inhibit glioma cell proliferation and immune evasion by suppressing the PI3K/

Table 3 Multivariate and univariate Cox regression analysis of prognosis in patients with LGG

Variable	Univariate analysis		Multivariate analysis	
	Exp (B)	P	Exp (B)	P
Age	0.939	0.881	–	–
Sex	0.608	0.257	–	–
Tumor location	0.520	0.168	–	–
Tumor number	2.493	0.097	3.783	0.02
Tumor diameter	0.711	0.418	–	–
Lymph node metastasis	2.456	0.032	2.590	0.03
WHO grade	2.345	0.060	2.263	0.08
SIGLEC8 expression	2.979	0.022	2.696	0.041

LGG, low-grade glioma; WHO, World Health Organization.

AKT signal transduction pathway (19). Moreover, Runx1 promotes glioma cell development by regulating the JAK-STAT signal transduction pathway (20). Finally, the PD-1 and JAK/STAT signaling pathways have been extensively studied in tumor immunotherapy (21,22). The involvement of *SIGLEC8* in these pathways supports its potential as a novel target for immunotherapy. Moreover, the role of *SIGLEC8* in the cell cycle and extracellular matrix indicates its potential impact on tumor cell proliferation and invasion. These findings provide direction for further research on the function of *SIGLEC8* in LGG and suggest its potential as a novel therapeutic target.

Our study included 72 patients with LGG, and qRT-PCR showed that *SIGLEC8* expression was upregulated in LGG tumor tissues. This upregulation was strongly correlated with the number of tumors and lymph node metastasis, suggesting that high *SIGLEC8* expression may promote the development and progression of LGG. This finding aligns with the results of the bioinformatics analysis mentioned above. Subsequent multivariate Cox regression analysis indicated that increased transcriptional activity of *SIGLEC8* is an independent risk factor for mortality in patients with LGG, implying that *SIGLEC8* expression is strongly correlated with the survival of patients with LGG and may potentially serve as an auxiliary prognostic assessment marker.

However, some limitations to our study should be noted. First, this study's sample size was relatively small and may not comprehensively represent the larger population of patients with LGG. Future studies should expand the sample size to validate our conclusions. Additionally, we did not conduct in-depth mechanistic experiments to verify nature of the relationship between *SIGLEC8* and the incidence and progression of LGG. Future research should include both *in vivo* and *in vitro* experiments, such as gene knockout or overexpression studies, to further clarify and investigate the function of *SIGLEC8* and the specific mechanisms and related signaling pathways.

Conclusions

This study found that *SIGLEC8* is a key prognostic marker for LGG, and its high expression is associated with poor survival outcomes. Moreover, *SIGLEC8* is involved in critical signaling pathways such as JAK/STAT and PI3K. This suggests that *SIGLEC8* can not only serve as a prognostic biomarker for LGG patients but also holds potential as a novel therapeutic target. Targeting *SIGLEC8* could open new avenues for immunotherapy or molecular targeted therapy in LGG patients, providing new insights for the development of personalized treatment strategies.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1662/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1662/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1662/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Longgang Central Hospital of Shenzhen (No. 2023ECPJ103) and informed consent was taken from all the patients or their families.

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