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Association of *Mitochondrial ribosomal protein S33* expression with poor prognosis in glioma

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Abstract

Despite advancements in diagnostic and therapeutic strategies, early detection and improved prognosis of gliomas remain challenging. A deeper understanding of glioma pathogenesis and the identification of reliable biomarkers are crucial for early diagnosis and the reduction of healthcare costs. Mitochondrial ribosomal protein S33 (MRPS33), a key component of mitochondrial protein synthesis, has not been well-characterized in terms of its expression profile, prognostic significance, and immunological relevance in glioma. This study aims to elucidate these aspects through bioinformatics analyses utilizing data from The Cancer Genome Atlas, Genotype-Tissue Expression Project, and Tumor Immune Estimation Resource databases through the Sangerbox platform. Our results indicate a pronounced upregulation of *MRPS33* in glioma tissues, which is significantly associated with poor prognosis, heightened immune cell infiltration, and differential drug sensitivities. Furthermore, functional enrichment analyses suggest that *MRPS33* is intricately involved in several key biological processes, thereby underscoring its potential role in glioma pathophysiology. In conclusion, our findings support the potential of *MRPS33* as a prognostic biomarker and therapeutic target in glioma, providing insights that may advance our understanding of disease mechanisms and inform future clinical strategies.

Keywords: *MRPS33*; Glioma; Prognosis; Immune cell infiltration

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1. Introduction

Glioma, which encompasses both glioblastoma multiforme (GBM) and lower-grade glioma (LGG), stands as one of the most significant and challenging diseases impacting human health across the globe, with a notably higher incidence observed in men than in women.[1,2] Patients afflicted with this condition frequently experience a range of distressing symptoms, including persistent headaches, seizures, and cognitive impairments, all of which can severely diminish quality of life.[3] Although prior research has identified associations between glioma and risk factors such as ionizing radiation exposure and certain genetic predispositions, the precise mechanisms driving glioma pathogenesis remain largely elusive and poorly understood.[4,5] Despite continuous advancements in diagnostic tools and therapeutic interventions, significant hurdles persist, particularly in early detection and improving patient prognosis, both of which

have seen only marginal progress over recent decades.[6-8] These limitations underscore the urgent need to investigate glioma pathogenesis more thoroughly and to identify robust biomarkers that can facilitate early diagnosis, improve prognostic accuracy, and ultimately reduce medical costs associated with this formidable disease.

The mitochondrial ribosomal small subunit (MRPS) family has emerged as a promising group of cancer-related biomarkers, providing valuable insights into the complex mechanisms underlying tumor development and progression.[9-12] Furthermore, these ribosomal components play a crucial role in the regulation of cell fate by influencing apoptosis and other cellular processes that govern cell survival and death pathways.[13] Among the members of this family, mitochondrial ribosomal protein S33 (MRPS33) stands out as a highly conserved protein essential for mitochondrial protein synthesis – an activity central to mitochondrial function, often described as the cell's powerhouse.[14] Notably, MRPS33 has been linked to various health conditions, including sleep apnea, and has been associated with healthy substance density in children,[15,16] indicating its potential importance in developmental biology. In addition, MRPS33 is considered essential for the intricate processes involved in tumorigenesis, highlighting its relevance in cancer biology.[17] Despite these established associations, a conspicuous gap remains in the literature: no studies have yet reported on the specific involvement of MRPS33 in glioma, a form of brain tumor that poses considerable challenges in treatment and understanding of its underlying biology.

In this study, we investigated the associations between *MRPS33* expression and various clinical and molecular features of glioma to determine its prognostic significance. Moreover, we conducted functional enrichment analyses to explore the potential biological roles of MRP33 in glioma progression.

2. Methods

2.1. Analysis of *MRPS33* expression in human cancer

Clinical data and RNA sequencing (RNA-seq) gene expression data from The Cancer Genome Atlas (TCGA) were analyzed using Sangerbox 3.0[18] (http://sangerbox.com/) and the Xiantao platform (https://www.xiantao.love/). Following the exclusion of data with missing clinical details, we included 529 LGG and 174 GBM samples for further analysis. Gene expression data were obtained in transcripts per million (TPM) format and normalized using $\log_2$(TPM+1) transformation. Normal tissue expression data were obtained from the Genotype-Tissue Expression (GTEx) database, version V8, with further details available on the official GTEx website (https://gtexportal.org/home/datasets).[19] Differential gene expression between normal and tumor samples was analyzed using the DESeq2 package.[20,21] Additional gene expression datasets (GSE16011 and GSE61335) were retrieved from the Gene Expression Omnibus (GEO) database (https://www.ncbi.nlm.nih.gov/geo/), a public repository of array- and sequence-based genomic data.

2.2. Prognostic and clinical correlation analysis of *MRPS33* in glioma

Tumor samples were divided into high and low *MRPS33* expression groups based on the median (50%) cutoff using the Xiantao platform. The survival package in R was used to examine the proportional hazards assumption and conduct Cox regression analysis. The rms package was used to construct and visualize nomogram models for clinical prediction.

2.3. Immune infiltration analysis of *MRPS33* in glioma

Immune infiltration was assessed using the single-sample gene set enrichment analysis algorithm provided in the GSVA R package (version 1.46.0),[22] based on 24 immune cell-type gene markers derived from a published immunology study.[23] RNA-seq data from the TCGA-Glioma project (https://portal.gdc.cancer.gov), processed using the STAR pipeline, were used for this analysis.

2.4. MRPS33 interaction networks

Gene–gene and protein–protein interaction networks for MRPS33 were generated using GeneMANIA[24] and STRING,[25] respectively.

2.5. Statistical analysis

Group differences were evaluated using Student's *t*-test. $p<0.05$ was considered statistically significant.

3. Results

3.1. *MRPS33* expression across cancers

MRPS33 expression was analyzed using data from the TCGA database. Elevated *MRPS33* expression was observed in 15 cancer types, including GBM and LGG (Figure 1A). On integration of TCGA and GTEx datasets, *MRPS33* expression was found to be significantly upregulated in gliomas (both GBM and LGG) as well as in 25 other cancer types (Figure 1B). These findings suggest that *MRPS33* is broadly dysregulated across multiple tumor types, including GBM and LGG, and may play a critical role in tumor progression.

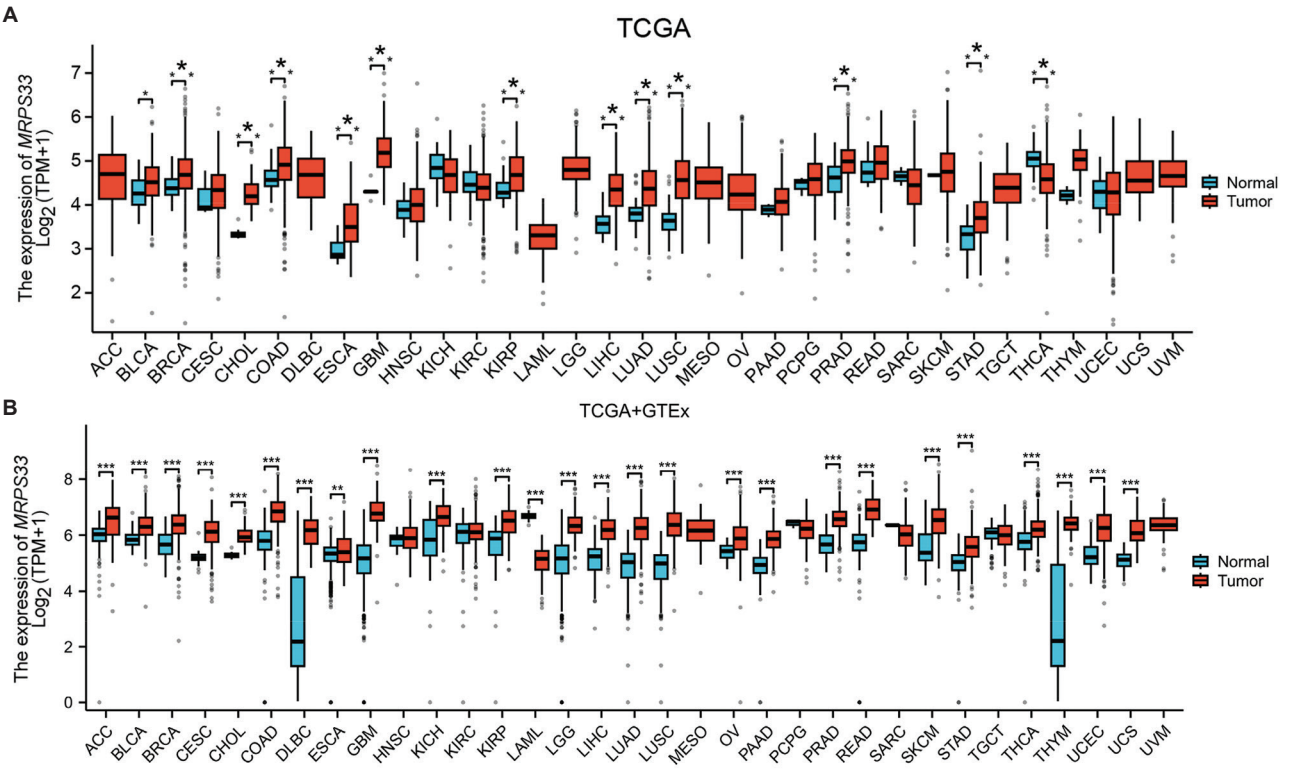

Figure 1. *MRPS33* mRNA expression in tumor and normal tissues. (A and B) *MRPS33* expression in pancancer analysis through (A) The Cancer Genome Atlas (TCGA) and (B) TCGA+ Genotype-Tissue Expression databases. Differential gene expression between normal and tumor samples was assessed using DESeq2.
Notes: ns: $p>0.05$; *$p<0.05$; **$p<0.01$; ***$p<0.001$.
Abbreviation: MRPS33: Mitochondrial ribosomal protein S33

3.2. *MRS33* as an independent prognostic factor for glioma

MRPS33 expression was further assessed using GEO datasets, which confirmed its elevated expression in glioma samples (Figure 2A and B). We then analyzed the relationship between *MRPS33* expression and glioma clinical features using TCGA data. High *MRPS33* expression was significantly associated with higher World Health Organization (WHO) grade, isocitrate dehydrogenase (IDH) mutation status, histological subtype, and older age (Figure 2C-F).

Survival analysis of glioma patients in the TCGA cohort revealed that lower *MRPS33* expression was associated with improved overall survival (OS), disease-specific survival (DSS), and progression-free interval (PFI) (Figure 2G-I). In addition, subgroup analyses that patients with high *MRPS33* expression – regardless of 1p/19q codeletion status, race (White), age (≤60), or gender, had poor prognoses (Figure 2J-N). Both univariate and multivariate Cox regression analyses indicated that WHO grade, IDH mutation status, histological subtype, gender, primary therapy outcome, and *MRPS33* expression were significantly correlated with OS (Table 1).

To further assess the potential of *MRPS33* as a glioma biomarker, we examined its correlation with other established glioma biomarkers[26] and found that *MRPS33* expression was positively correlated with these markers (Figure 3). A prognostic nomogram was constructed using data from the TCGA glioma cohort to predict OS, DSS, and PFI, incorporating pathological stage and *MRPS33* expression as prognostic factors (Figure 4A-C). Based on calibration curves, the glioma nomogram demonstrated good predictive performance for glioma patient outcomes at 1, 3, and 5 years (Figure 4D-F). These compelling results further underscore the promising potential of *MRPS33* as a valuable glioma biomarker, suggesting its relevance in clinical applications and future research endeavors.

3.3. Correlation between *MRPS33* gene expression and immune cell infiltration in glioma

Given the critical and multifaceted role of immune cells in glioma progression[27,28] – a type of brain tumor – a thorough analysis was conducted to explore the intricate relationship between *MRPS33* expression and the infiltration of 24 distinct immune cell types. In the GBMLGG dataset, *MRPS33* expression was significantly correlated with 15

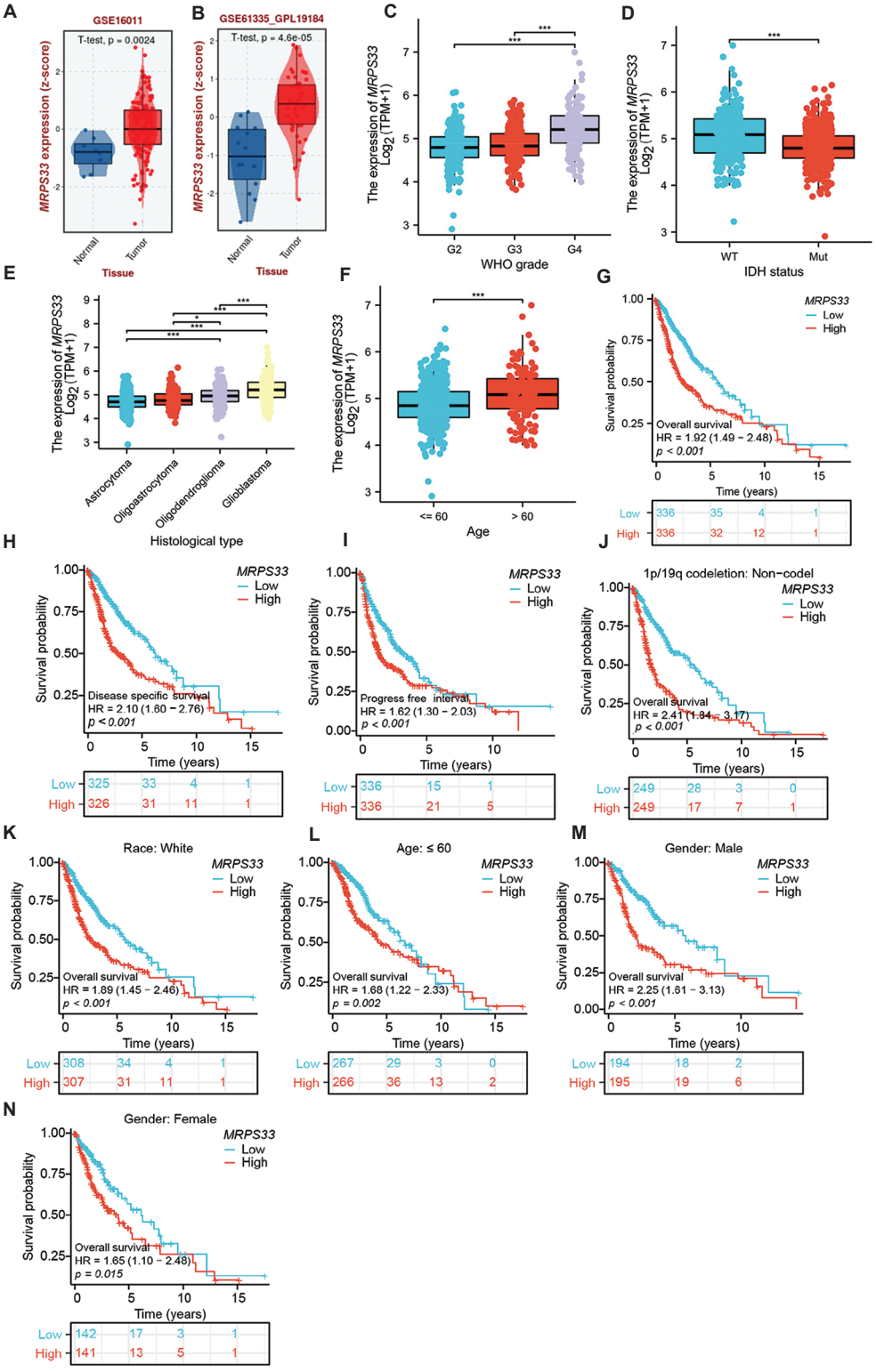

Figure 2. Expression and prognostic analysis of *MRPS33* in glioma. (A and B) Validation of *MRPS33* expression in glioma via the Gene Expression Omnibus dataset. (C-F) Correlation between *MRPS33* expression and clinical characteristics, including WHO grade (C), IDH mutation status (D), histological subtype (E), and age (F). (G-N) Correlations between *MRPS33* and survival or demographic variables, including overall survival (G), disease-free survival (H), progression-free interval (I), and 1p19q codeletion: noncodel (J), race (White) (K), age (J), and sex (M and N).

Notes: *p<0.05; **p<0.01; ***p<0.001.

Abbreviations: HR: Hazard ratio; MRPS33: Mitochondrial ribosomal protein S33; IDH: Isocitrate dehydrogenase.

Table 1. Univariate and multivariate Cox regression analyses of clinical characteristics associated with overall survival in glioma patients

Characteristics	Total (N)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	*p*-value	Hazard ratio (95% CI)	*p*-value
WHO grade	636				
G2	223	Reference		Reference	
G3	245	2.967 (1.986 – 4.433)	<0.001***	2.056 (1.297 – 3.259)	0.002**
G4	168	18.600 (12.448 – 27.794)	<0.001***	6.333 (2.010 – 19.952)	0.002**
IDH mutation status	688				
Wild type	246	Reference		Reference	
Mutant	442	0.116 (0.089 – 0.151)	<0.001***	0.374 (0.231 – 0.606)	<0.001***
Gender	698				
Female	297	Reference		Reference	
Male	401	1.250 (0.979 – 1.595)	0.073	2.089 (1.326 – 3.292)	0.002**
Primary therapy outcome	464				
PD	112	Reference		Reference	
SD	148	0.440 (0.294 – 0.658)	<0.001***	0.412 (0.248 – 0.684)	<0.001***
PR	65	0.167 (0.073 – 0.385)	<0.001***	0.199 (0.071 – 0.558)	0.002**
CR	139	0.131 (0.063 – 0.273)	<0.001***	0.167 (0.078 – 0.361)	<0.001***
MRPS33	698	2.245 (1.744 – 2.890)	<0.001***	1.282 (0.755 – 2.179)	0.358

Notes: *p<0.05, **p<0.01, ***p<0.001.
Abbreviations: CR: Complete response; IDH: Isocitrate dehydrogenase; PD: Progressive disease; PR: Partial response; SD: Stable disease; WHO grade: World Health Organization grade.

major immune cell types (Figure 5A). Specifically, *MRPS33* expression was negatively correlated with memory T cells, central memory T cells, and natural killer cells, gamma delta T cells, follicular helper T cells, plasmacytoid dendritic cells, and $CD8^+$ T cells, and regulatory T cells (Figure 5B-I). The observed diversity of both tumor and immune cell populations suggests that *MRPS33* expression in glioma may vary significantly from its expression in various immune cell types. This highlights the complexity of the tumor microenvironment and underscores the potential implications for targeted immunotherapeutic strategies.

3.4. Gene interaction network of *MRPS33* in glioma

The protein and gene interaction networks of MRPS33 across cancers are shown in Figure 6A and B. We further examined the correlation between *MRPS33* expression and that of several interacting genes specifically in glioma. This analysis uncovered significant positive correlations with *LSM3*, *MRPS23*, *MRPL13*, and *MTIF2* (Figure 6C). Notably, these genes were highly expressed in glioma cases, and patients with elevated expression levels of these genes exhibited significantly worse prognoses (Figure 6D-E).

3.5. Functional analysis of *MRPS33* in glioma

To elucidate the functional role of *MRPS33* in glioma, we performed a correlation analysis using LinkedOmics.[29] A heatmap was generated to illustrate genes mostly strongly correlated with *MRPS33* expression (Figure 7A and B). The Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis indicated significant involvement in oxidative phosphorylation, ribosome, Parkinson's disease, phosphorylation signaling cascades, and inositol phosphate metabolism (Figure 7C). Gene ontology (GO) annotation further revealed that the correlated genes are involved in translational elongation, mitochondrial gene expression, mitochondrial respiratory complex assembly, glutamate receptor signaling, and trans-synaptic regulation (Figure 7D).

3.6. Drug sensitivity analysis of *MRPS33*

Using the gene set cancer analysis platform,[30] we assessed the correlation between *MRPS33* expression and drug sensitivity based on data from the Genomics of Drug Sensitivity in Cancer (GDSC)[31] and Cancer Therapeutics Response Portal (CTRP)[32] databases. According to the GDSC analysis, *MRPS33* expression was positively correlated with sensitivity to several drugs,

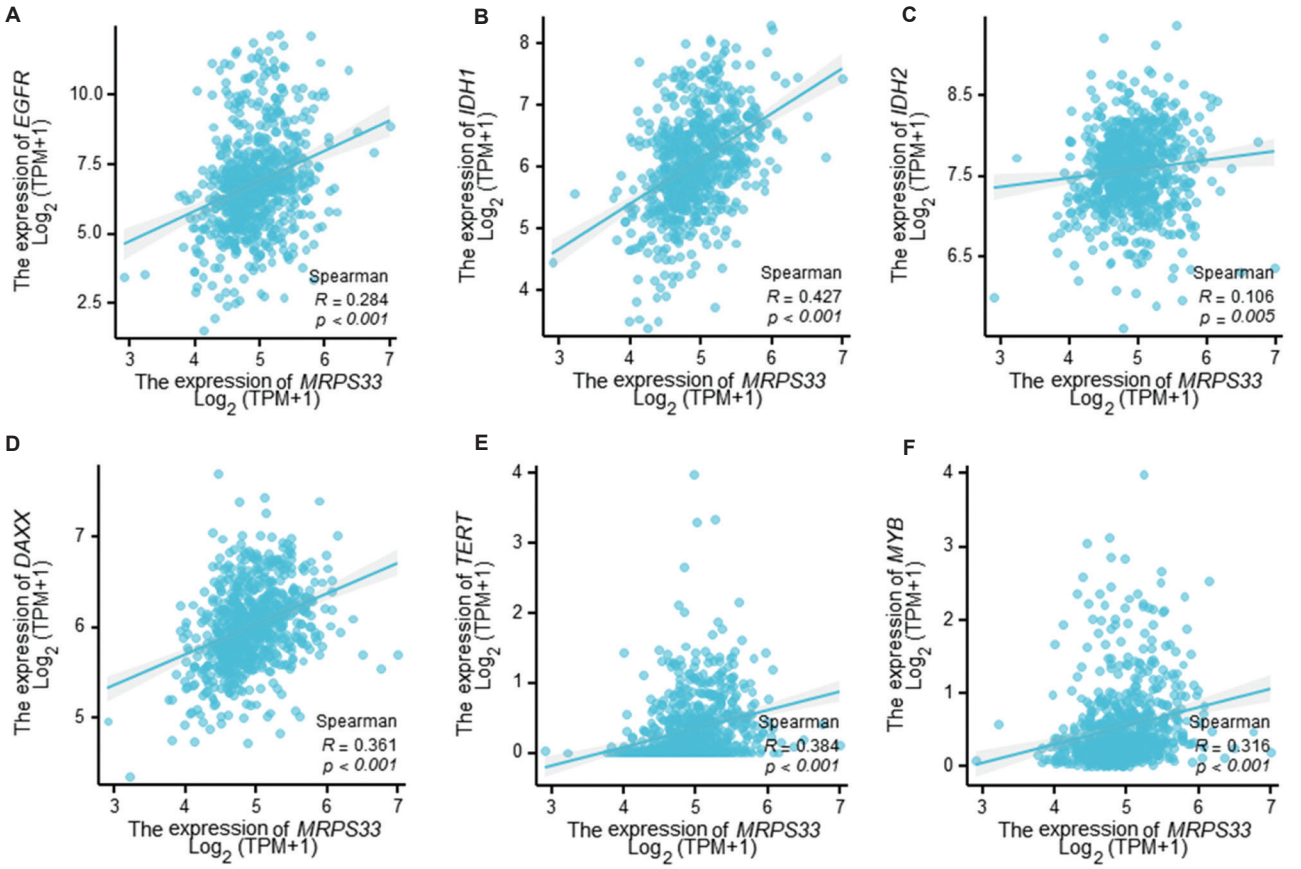

Figure 3. Correlation between *MRPS33* expression and established glioma biomarkers. (A-F) Correlation between *MRPS33* expression and the expression of *EGFR* (A), *IDH1* (B), *IDH2* (C), *DAXX* (D), *TERT* (E), and *MYB* (F).
Abbreviation: MRPS33: Mitochondrial ribosomal protein S33.

including dasatinib, olaparib, RG-108, and daporinad, indicating that elevated *MRPS33* expression may enhance the therapeutic efficacy of these compounds. Conversely, MRPS33 expression showed a negative correlation with sensitivity to other compounds such as HBX-41108, GW-405833, STF-31, and marinopyrrole A, suggesting that increased MRPS33 expression could potentially diminish the effectiveness of these particular drugs (Figure 8A). In parallel, analysis using the CTRP database revealed that *MRPS33* expression was positively correlated with increased sensitivity to multiple chemotherapeutic agents, including bleomycin (50 μM), BX-795, olaparib, RO-3306, camptothecin, and docetaxel. These results further support the notion that MRPS33 may play a significant role in mediating drug response. However, *MRPS33* expression was negatively associated with sensitivity to dabrafenib and PLX4720, indicating a complex and potentially context-dependent relationship between *MRPS33* expression and drug efficacy (Figure 8B).

4. Discussion

Gliomas remain one of the most challenging tumors in neuro-oncology, necessitating continued research into their pathogenesis, early detection, and innovative therapeutic approaches aimed at enhancing patient outcomes. The identification of novel cancer biomarkers and therapeutic targets is critical, and bioinformatics analysis of tumor datasets is of paramount importance, as it provides critical insights into the molecular underpinnings of various malignancies.[33-35]

In pediatric populations, *MRPS33* has previously been significantly associated with bone mineral density and lean body mass,[16] as well as with the development of sleep-disordered breathing phenotypes.[15] However, there has been a conspicuous lack of studies investigating the potential role of *MRPS33* in glioma prognosis or immune regulation.

In our research, we discovered that *MRPS33* expression was notably upregulated across a wide array of cancer

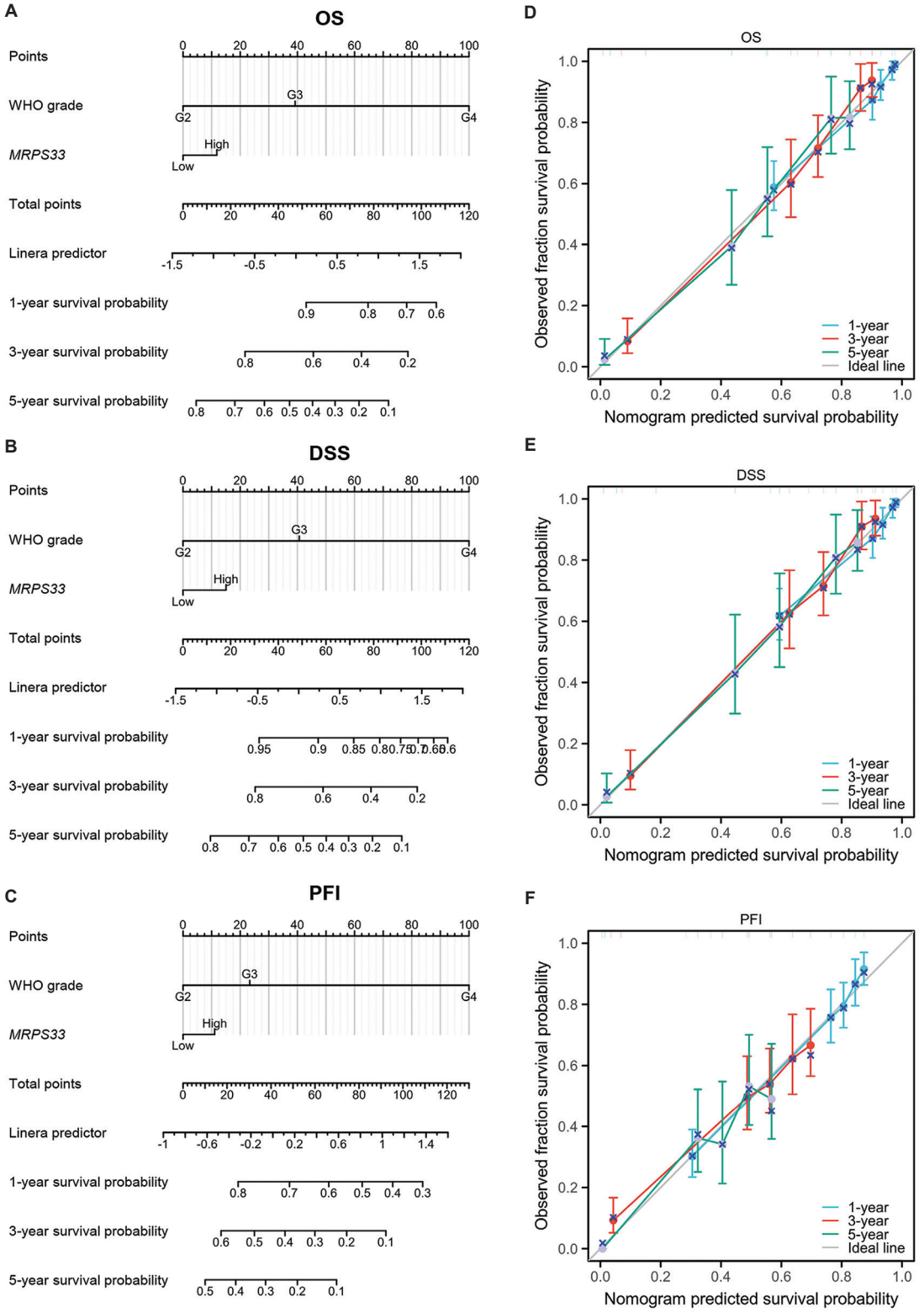

Figure 4. Nomogram and calibration curves for predicting 1-, 3-, and 5-year survival outcomes in glioma patients. (A-C) Nomogram integrating *MRPS33* and other prognostic factors to predict overall survival, disease-free survival, and progression-free interval in glioma patients based on The Cancer Genome Atlas data. (D-E) Calibration curves comparing predicted survival probabilities (X-axis) with actual observed outcomes (Y-axis).
Abbreviation: MRPS33: Mitochondrial ribosomal protein S33.

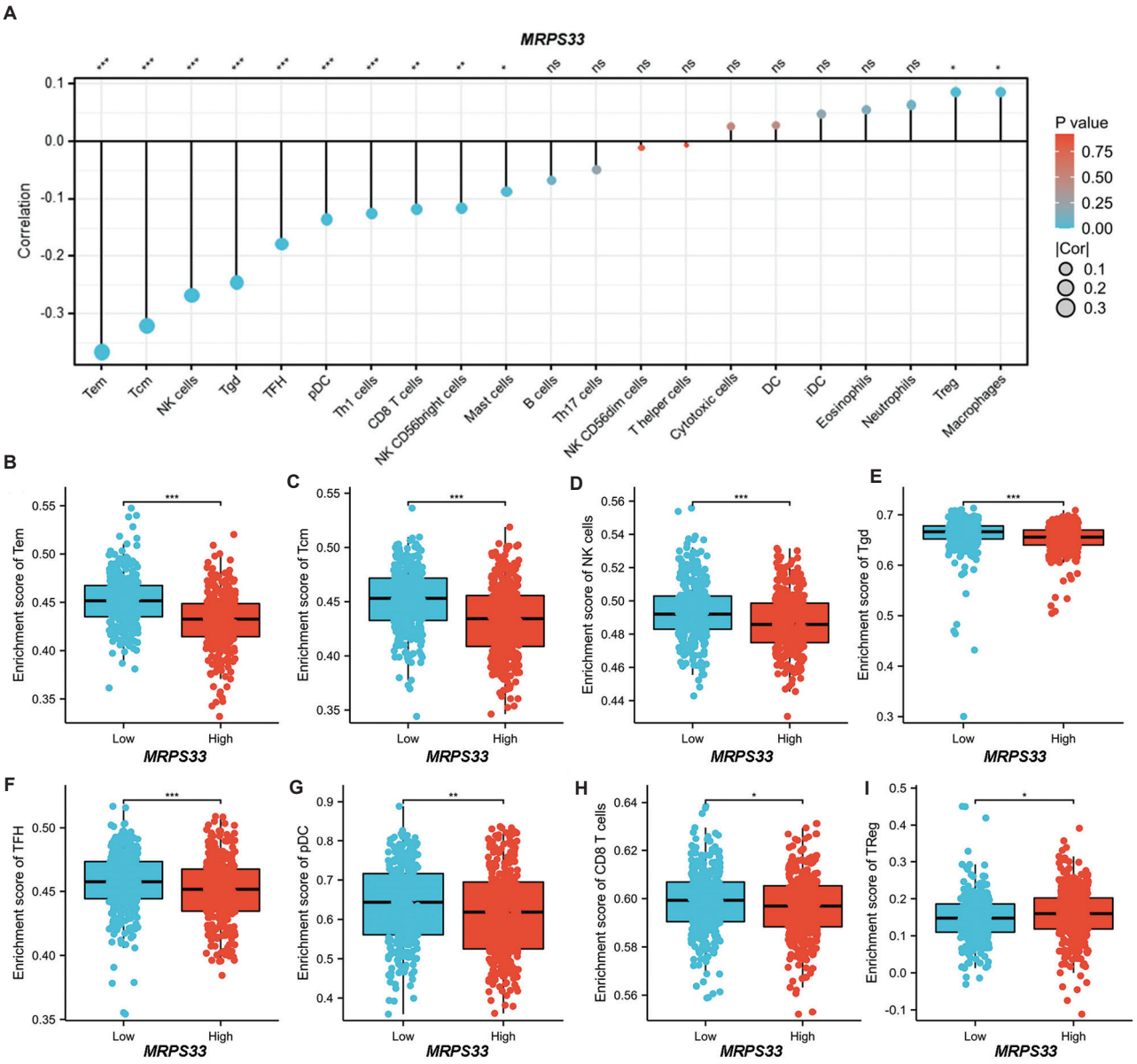

Figure 5. Correlation between *MRPS33* expression and immune cell infiltration in glioma. (A) Correlation between *MRPS33* expression and immune cell infiltration levels using the Tumor Immune Estimation Resource database. (B-I) Correlations between *MRPS33* expression and specific immune cell types: effector memory T cells (Tem) (B), central memory T cells (Tcm) (C), natural killer cells (D), gamma delta T cells (E), follicular helper T cells (F), plasmacytoid dendritic cells (G), $CD8^+$ T (H), and regulatory T cells (I). Notes: *p<0.05, **p<0.01, ***p<0.001.
Abbreviation: MRPS33: Mitochondrial ribosomal protein S33.

types, including glioma. Higher *MRPS33* expression was significantly correlated with poorer OS, DSS, and PFI in patients diagnosed with glioma. These compelling results clearly suggest that MRPS33 may play a pivotal role in the pathophysiology of glioma. Furthermore, calibration curves and nomogram analyses reinforced the predictive value of *MRPS33* in clinical prognosis.

Collectively, our findings support the view that the MRPS family, of which MRPS33 is a member, holds considerable promise as a group of tumor markers in the ongoing quest for effective cancer diagnostics and therapeutics.[9-12]

Gliomas account for approximately 81% of all malignancies affecting the central nervous system,

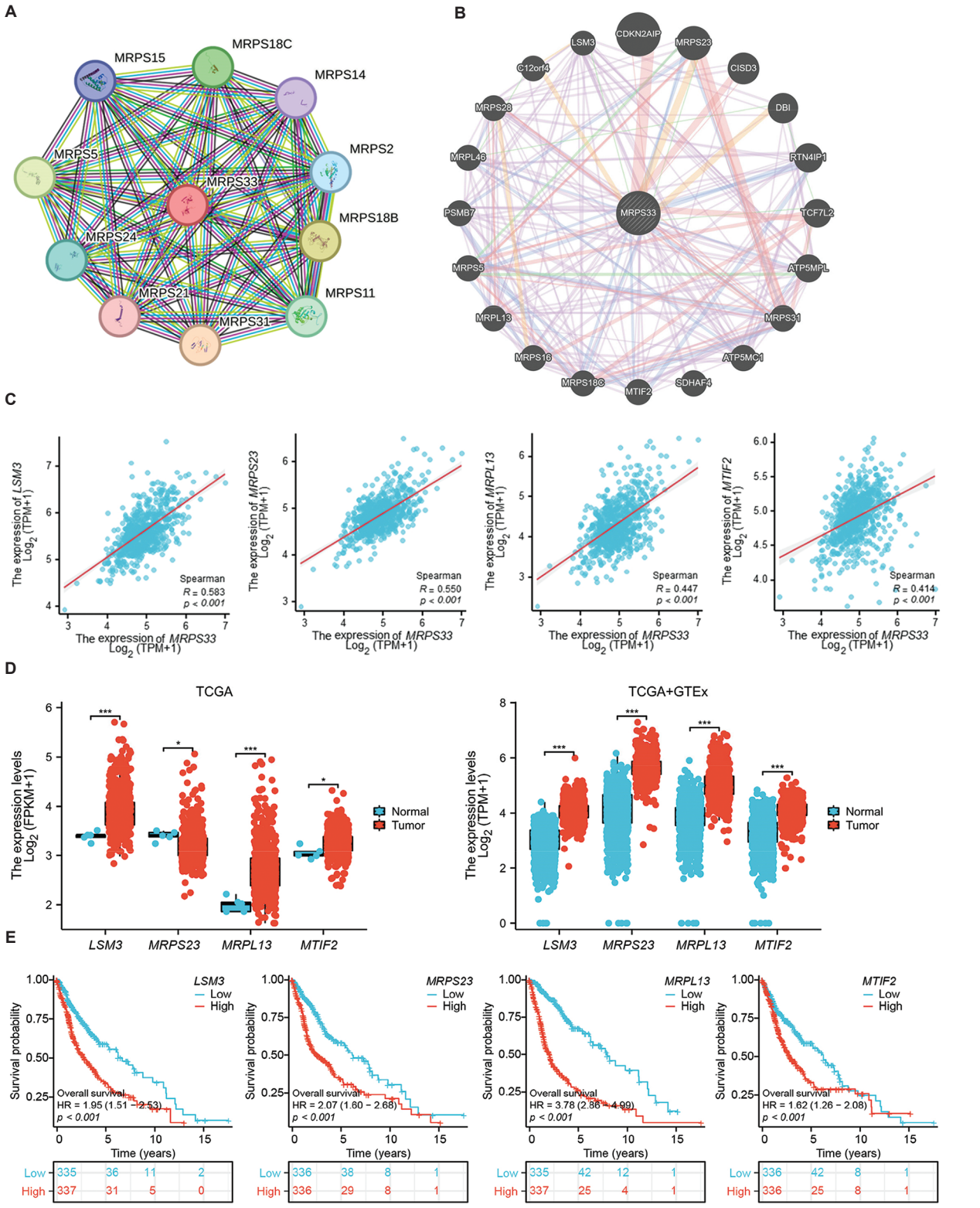

Figure 6. Interaction network analysis of *MRPS33*.(A and B) MRPS33 interaction network at the protein (A) and gene (B) levels across multiple cancers. (C) Correlations between *MRPS33* expression and *LSM3*, *MRPS23*, *MRPL13*, and *MTIF2* in glioma. (D-E) Expression levels and prognostic significance of *LSM3*, *MRPS23*, *MRPL13*, and *MTIF2* in glioma.

Notes: *p<0.05, **p<0.01, ***p<0.001.

Abbreviations: TCGA: The Cancer Genome Atlas; GTEx: Genotype-Tissue Expression; MRPS33: Mitochondrial ribosomal protein S33.

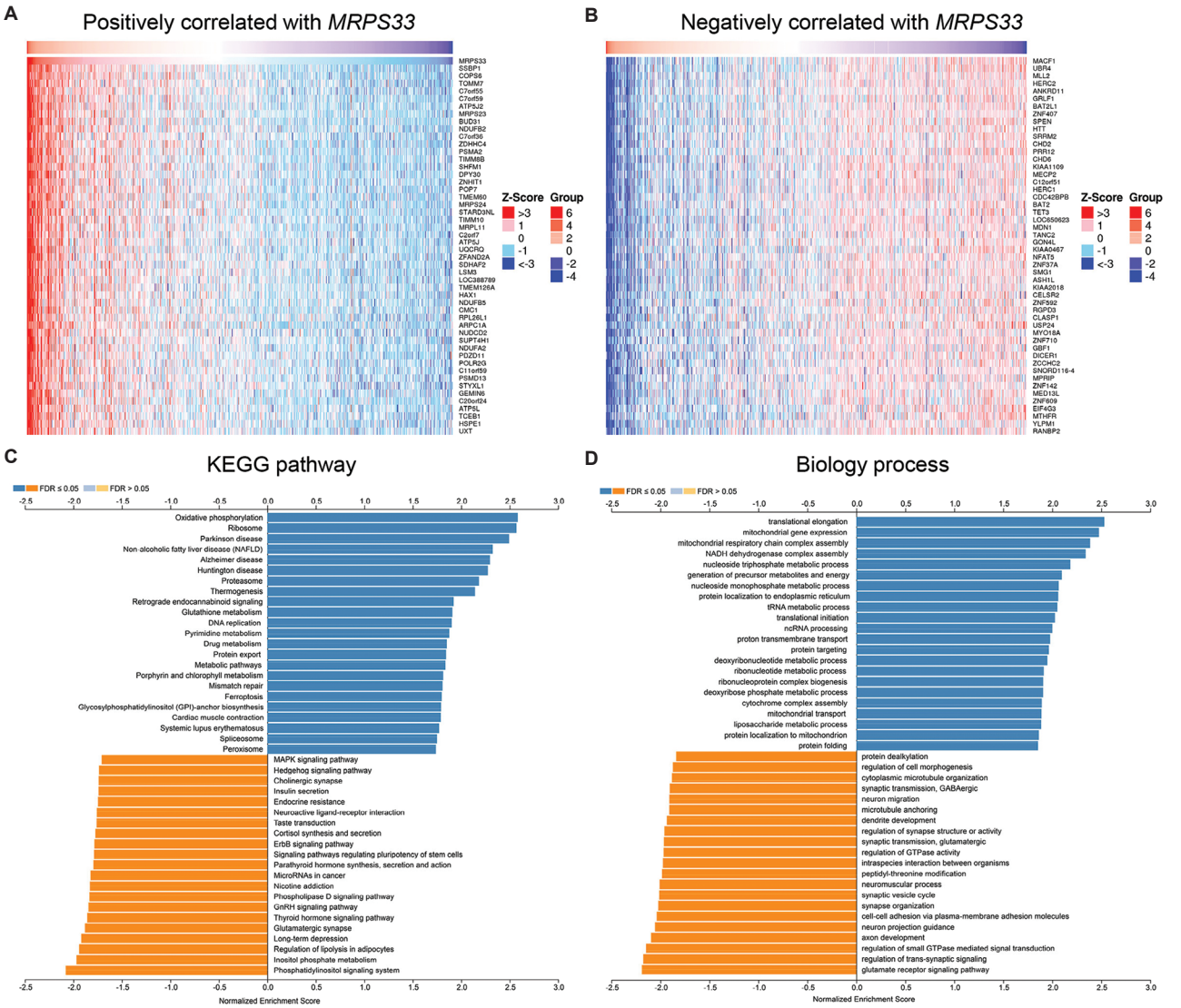

Figure 7. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and gene ontology (GO) enrichment analyses of *MRPS33*-related genes in glioma. (A and B) Heatmaps showing the top 50 genes positively (A) and negatively (B) correlated with *MRPS33*. (C and D) KEGG pathway (C) and GO biological process (D) enrichment analyses for *MRPS33*-related genes.
Abbreviations: FDR: False discovery rate; MRPS33: Mitochondrial ribosomal protein S33.

underscoring their clinical significance. Over the past decade, the advent of immunotherapy has dramatically reshaped the treatment landscape for various tumors, offering new hope and strategies for combating these challenging conditions.[36] However, the intricate interaction between gliomas and immune infiltration remains complex and incompletely understood, presenting both significant challenges and promising opportunities for researchers and clinicians alike.[37]

The glioma microenvironment, a specific form of the tumor microenvironment, is characterized by a pronounced state of immunosuppression, primarily driven by tumor-associated macrophages and microglia (TAMs). These cells can constitute a staggering 30 – 50% of the tumor's cellular population. TAMs play a critical role in suppressing T-cell activity through the secretion of immunosuppressive cytokines, including transforming growth factor-beta and interleukin-10, while simultaneously promoting angiogenesis and tumor invasion. Furthermore, additional components such as immune checkpoint molecules, myeloid-derived suppressor cells, and regulatory T cells, and highly expressed programmed death-ligand 1 contribute to a network of immunosuppressive mechanisms that significantly hinder the antitumor immune response.[38-40]

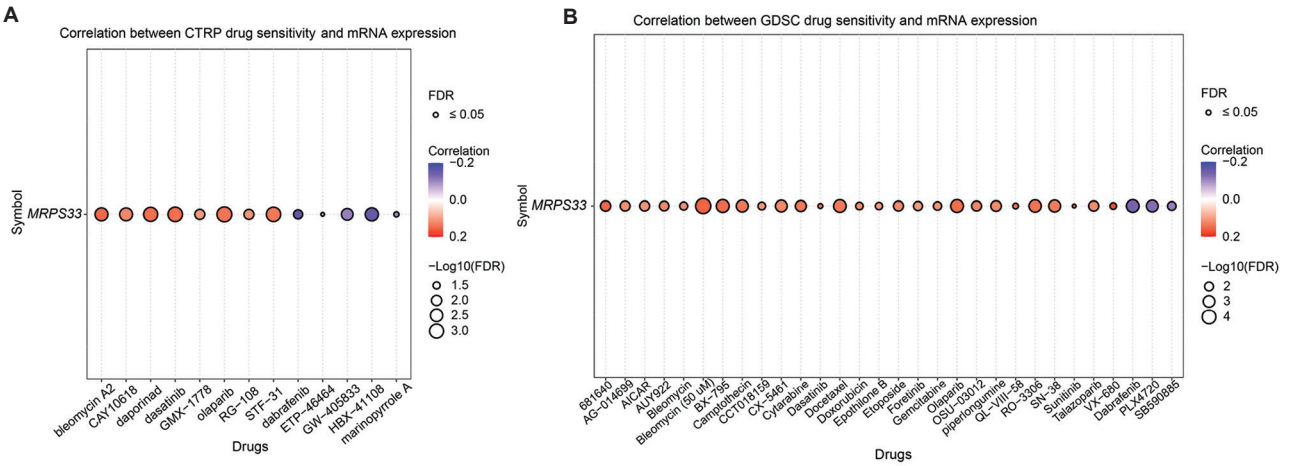

Figure 8. Drug sensitivity analysis of MRPS33. (A and B) Analysis of human cancer CTRP (A) and GDSC (B) data for the correlation between MRPS33 expression and drug sensitivity.
Abbreviations: CTRP: Cancer Therapeutics Response Portal; FDR: False discovery rate; GDSC: Genomics of Drug Sensitivity in Cancer; MRPS33: Mitochondrial ribosomal protein S33.

Although cytotoxic T cells and natural killer cells are present within the glioma microenvironment, their numbers and functional capacity are typically insufficient to mount an effective immune response against tumor progression.[38] In addition, the immune evasion mechanisms employed by gliomas significantly exacerbate treatment challenges, posing a formidable barrier to effective therapeutic intervention.[39,41] This dual mechanism – comprising both immune suppression and immune evasion – enables gliomas to grow unchecked and resist conventional therapeutic approaches that may be effective in other cancer types.

In our comprehensive study, we found that *MRPS33* expression was significantly associated with the infiltration levels of 15 major immune cell types within the glioma microenvironment. This suggests a potential link between *MRPS33* expression and immune modulation in glioma. Notably, *MRPS33* expression was negatively correlated with several immune cell populations, including central memory T cells, effector memory T cells, natural killer cells, gamma delta T cells, follicular helper T cells, plasmacytoid dendritic cells, $CD8^+$ T cells, and regulatory T cells. To the best of our knowledge, this study represents the first exploration linking the MRPS family to tumor therapy from an immunological perspective, highlighting the potential significance of *MRPS33* in this context. Our findings suggest that *MRPS33* could serve as a crucial regulatory factor within the realm of immunotherapy, warranting further in-depth investigation into its functional roles and therapeutic implications.

To gain a deeper understanding of the intricate role that *MRPS33* plays in the context of glioma, we conducted a series of comprehensive analyses, which included gene–gene interaction mapping, KEGG pathway analysis, and GO enrichment assessments. Our research revealed 20 genes that interact with *MRPS33*, with significant positive correlations observed between *MRPS33* and *LSM3*, *MRPS23*, *MRPL13*, and *MTIF2*. It is noteworthy that *MRPS23*, another member of the MRPS gene family, has been shown to facilitate breast cancer metastasis and diminish sensitivity to CDK1 inhibitors, highlighting its critical role in cancer progression.[42,43] Furthermore, a recent study has identified *MRPS23* as a promising prognostic biomarker for glioma, underscoring its clinical relevance.[44] These findings collectively suggest that *MRPS33* may also exert multiple functional roles within the glioma microenvironment. In addition, our functional enrichment analysis indicated that *MRPS33*-associated genes in glioma are intricately involved in several biological processes, including oxidative phosphorylation, ribosome function, the pathophysiology of Parkinson's disease, phosphorylation signaling cascades, inositol phosphate metabolism, translational elongation, mitochondrial gene expression, mitochondrial respiratory complex assembly, the glutamate receptor signaling pathway, and trans-synaptic regulation. Importantly, many of these signaling pathways have previously been implicated in the regulation of malignant glioma phenotypes.[45]

Finally, our data revealed a significant relationship between *MRPS33* expression and sensitivity to a diverse array of antineoplastic drugs, further emphasizing the considerable potential of *MRPS33* in tumor treatment and therapeutic strategy development.

However, it is important to note that this research is strictly confined to the realm of bioinformatics, and as such, it carries inherent limitations. Looking ahead, it will be crucial to further validate *MRPS33* expression in glioma through both *in vitro* and *in vivo* experiments. These studies will provide a clearer understanding of the role *MRPS33* which plays in regulating the malignant phenotype associated with glioma. In addition, we aim to elucidate the biological mechanisms underlying *MRPS33* activity. It is also essential to investigate the potential connections between *MRPS33* and the immune microenvironment, as well as its impact on drug sensitivity, both of which require thorough experimental validation. In future research, we will concentrate on designing and implementing relevant experiments to analyze these critical issues in greater detail. This will enhance the depth and robustness of our research, solidify our conclusions, and ultimately provide a robust theoretical foundation for the continued development of *MRPS33* as a promising tumor marker.

5. Conclusion

A comprehensive bioinformatic investigation of *MRPS33* has provided valuable insights into its potential role in glioma prognosis and diagnosis. These findings support the possibility of *MRPS33* serving as a reliable biomarker. Furthermore, this extensive analysis could pave the way for the future development of *MRPS33* as a therapeutic target, with the potential to improve patient outcomes and advance the field of neuro-oncology.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Zhongmin Li, Xinxing Wang
Data curation: Zhongmin Li, Xiangyang Wang
Investigation: Zhongmin Li
Methodology: Zhongmin Li
Supervision: Zhongmin Li, Qiang Li
Writing–original draft: Zhongmin Li, Qiang Li
Writing–review & editing: All authors

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

All data from the study are presented in the article, and the data from this article can be obtained from the public database, The Cancer Genome Atlas (https://portal.gdc.cancer.gov/).

References

1. Lin MD, Tsai AC, Abdullah KG, McBrayer SK, Shi DD. Treatment of IDH-mutant glioma in the INDIGO era. *NPJ Precis Oncol*. 2024;8(1):149.

   doi: 10.1038/s41698-024-00646-2

2. Yin J, Liu G, Zhang Y, *et al*. Gender differences in gliomas: From epidemiological trends to changes at the hormonal and molecular levels. *Cancer Lett*. 2024;598:217114.

   doi: 10.1016/j.canlet.2024.217114

3. Wei Y, Xu Y, Sun Q, *et al*. Targeting ferroptosis opens new avenues in gliomas. *Int J Biol Sci*. 2024;20(12):4674-4690.

   doi: 10.7150/ijbs.96476

4. Agnihotri TG, Salave S, Shinde T, *et al.* Understanding the role of endothelial cells in brain tumor formation and metastasis: A proposition to be explored for better therapy. *J Natl Cancer Cent*. 2023;3(3):222-235.

   doi: 10.1016/j.jncc.2023.08.001

5. Nicholson JG, Fine HA. Diffuse glioma heterogeneity and its therapeutic implications. *Cancer Discov*. 2021;11(3):575-590.

   doi: 10.1158/2159-8290.CD-20-1474

6. Dai F, Yuan Y, Hao J, *et al*. PDCD2 as a prognostic biomarker in glioma correlates with malignant phenotype. *Genes Dis*. 2024;11(5):101106.

   doi: 10.1016/j.gendis.2023.101106

7. Kros JM, Mustafa DM, Dekker LJ, Sillevis Smitt PA, Luider TM, Zheng PP. Circulating glioma biomarkers. *Neuro Oncol*. 2015;17(3):343-360.

   doi: 10.1093/neuonc/nou207

8. Lukas RV, Wainwright DA, Horbinski CM, Iwamoto FM, Sonabend AM. Immunotherapy against gliomas: Is the breakthrough near. *Drugs*. 2019;79(17):1839-1848.

   doi: 10.1007/s40265-019-01203-z

9. Bacon JM, Jones JL, Liu GS, Dickinson JL, Raspin K. Mitochondrial ribosomal proteins in metastasis and their potential use as prognostic and therapeutic targets. *Cancer*

Metastasis Rev. 2024;43(4):1119-1135.

doi: 10.1007/s10555-024-10216-4

10. Bao S, Wang X, Li M, *et al*. Potential of mitochondrial ribosomal genes as cancer biomarkers demonstrated by bioinformatics results. *Front Oncol*. 2022;12:835549.

doi: 10.3389/fonc.2022.835549

11. Lin X, Guo L, Lin X, Wang Y, Zhang G. Expression and prognosis analysis of mitochondrial ribosomal protein family in breast cancer. *Sci Rep*. 2022;12(1):10658.

doi: 10.1038/s41598-022-14724-7

12. Xie C, Hu J, Hu Q, Jiang L, Chen W. Classification of the mitochondrial ribosomal protein-associated molecular subtypes and identified a serological diagnostic biomarker in hepatocellular carcinoma. *Front Surg*. 2022;9:1062659.

doi: 10.3389/fsurg.2022.1062659

13. Huang G, Li H, Zhang H. Abnormal expression of mitochondrial ribosomal proteins and their encoding genes with cell apoptosis and diseases. *Int J Mol Sci*. 2020;21(22):8879.

doi: 10.3390/ijms21228879

14. Cheong A, Lingutla R, Mager J. Expression analysis of mammalian mitochondrial ribosomal protein genes. *Gene Expr Patterns*. 2020;38:119147.

doi: 10.1016/j.gep.2020.119147

15. Cade BE, Lee J, Sofer T, *et al*. Whole-genome association analyses of sleep-disordered breathing phenotypes in the NHLBI TOPMed program. *Genome Med*. 2021;13(1):136.

doi: 10.1186/s13073-021-00917-8

16. Xu J, Ma J, Zeng Y, *et al*. Transcriptome-wide association study identifies novel genes associated with bone mineral density and lean body mass in children. *Endocrine*. 2023;79(2):400-409.

doi: 10.1007/s12020-022-03225-2

17. Revathi Paramasivam O, Gopisetty G, Subramani J, Thangarajan R. Expression and affinity purification of recombinant mammalian mitochondrial ribosomal small subunit (MRPS) proteins and protein-protein interaction analysis indicate putative role in tumourigenic cellular processes. *J Biochem*. 2021;169(6):675-692.

doi: 10.1093/jb/mvab004

18. Shen W, Song Z, Zhong X, *et al*. Sangerbox: A comprehensive, interaction-friendly clinical bioinformatics analysis platform. *Imeta*. 2022;1(3):e36.

doi: 10.1002/imt2.36

19. Tomczak K, Czerwińska P, Wiznerowicz M. The cancer genome atlas (TCGA): An immeasurable source of knowledge. *Contemp Oncol (Pozn)*. 2015;19(1A):A68-A77.

doi: 10.5114/wo.2014.47136

20. Gillette MA, Satpathy S, Cao S, *et al*. Proteogenomic characterization reveals therapeutic vulnerabilities in lung adenocarcinoma. *Cell*. 2020;182(1):200-25.e35.

doi: 10.1016/j.cell.2020.06.013

21. Gao Q, Zhu H, Dong L, *et al*. Integrated proteogenomic characterization of HBV-related hepatocellular carcinoma. *Cell*. 2019;179(2):561-577.e22.

doi: 10.1016/j.cell.2019.08.052

22. Hänzelmann S, Castelo R, Guinney J. GSVA: Gene set variation analysis for microarray and RNA-seq data. *BMC Bioinformatics*. 2013;14:7.

doi: 10.1186/1471-2105-14-7

23. Bindea G, Mlecnik B, Tosolini M, *et al*. Spatiotemporal dynamics of intratumoral immune cells reveal the immune landscape in human cancer. *Immunity*. 2013;39(4):782-795.

doi: 10.1016/j.immuni.2013.10.003

24. Warde-Farley D, Donaldson SL, Comes O, *et al*. The GeneMANIA prediction server: Biological network integration for gene prioritization and predicting gene function. *Nucleic Acids Res*. 2010;38:W214-W220.

doi: 10.1093/nar/gkq537

25. Szklarczyk D, Gable AL, Lyon D, *et al*. STRING v11: Protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. *Nucleic Acids Res*. 2019;47(D1):D607-D613.

doi: 10.1093/nar/gky1131

26. Bou Zerdan M, Atoui A, Hijazi A, *et al*. Latest updates on cellular and molecular biomarkers of gliomas. *Front Oncol*. 2022;12:1030366.

doi: 10.3389/fonc.2022.1030366

27. Guo X, Sui R, Piao H. Exosomes-mediated crosstalk between glioma and immune cells in the tumor microenvironment. *CNS Neurosci Ther*. 2023;29(8):2074-2085.

doi: 10.1111/cns.14239

28. Sankowski R, Süß P, Benkendorff A, *et al*. Multiomic spatial landscape of innate immune cells at human central nervous system borders. *Nat Med*. 2024;30(1):186-198.

doi: 10.1038/s41591-023-02673-1

29. Vasaikar SV, Straub P, Wang J, Zhang B. LinkedOmics: Analyzing multi-omics data within and across 32 cancer types. *Nucleic Acids Res*. 2018;46(D1):D956-D963.

doi: 10.1093/nar/gkx1090

30. Liu CJ, Hu FF, Xie GY, *et al*. GSCA: An integrated platform for gene set cancer analysis at genomic, pharmacogenomic and immunogenomic levels. *Brief Bioinform*. 2023;24(1):bbac558.

doi: 10.1093/bib/bbac558

31. Yang W, Soares J, Greninger P, *et al*. Genomics of drug sensitivity in cancer (GDSC): A resource for therapeutic biomarker discovery in cancer cells. *Nucleic Acids Res*. 2013;41:D955-D961.

doi: 10.1093/nar/gks1111

32. Basu A, Bodycombe NE, Cheah JH, *et al*. An interactive resource to identify cancer genetic and lineage dependencies targeted by small molecules. *Cell*. 2013;154(5):1151-1161.

doi: 10.1016/j.cell.2013.08.003

33. Cortés-Ciriano I, Gulhan DC, Lee JJ, Melloni G, Park PJ. Computational analysis of cancer genome sequencing data. *Nat Rev Genet*. 2022;23(5):298-314.

doi: 10.1038/s41576-021-00431-y

34. Jiang P, Sinha S, Aldape K, Hannenhalli S, Sahinalp C, Ruppin E. Big data in basic and translational cancer research. *Nat Rev Cancer*. 2022;22(11):625-639.

doi: 10.1038/s41568-022-00502-0

35. Yang L, Wang J, Altreuter J, *et al*. Tutorial: Integrative computational analysis of bulk RNA-sequencing data to characterize tumor immunity using RIMA. *Nat Protoc*. 2023;18(8):2404-2414.

doi: 10.1038/s41596-023-00841-8

36. Xu S, Tang L, Li X, Fan F, Liu Z. Immunotherapy for glioma: Current management and future application. *Cancer Lett*. 2020;476:1-12.

doi: 10.1016/j.canlet.2020.02.002

37. Liu H, Zhao Q, Tan L, *et al*. Neutralizing IL-8 potentiates immune checkpoint blockade efficacy for glioma. *Cancer Cell*. 2023;41(4):693-710.e8.

doi: 10.1016/j.ccell.2023.03.004

38. Thomas BC, Staudt DE, Douglas AM, Monje M, Vitanza NA, Dun MD. CAR T cell therapies for diffuse midline glioma. *Trends Cancer*. 2023;9(10):791-804.

doi: 10.1016/j.trecan.2023.07.007

39. Fan X, Li J, Huang B, *et al*. Noninvasive radiomics model reveals macrophage infiltration in glioma. *Cancer Lett*. 2023;573:216380.

doi: 10.1016/j.canlet.2023.216380

40. Wei J, Marisetty A, Schrand B, *et al*. Osteopontin mediates glioblastoma-associated macrophage infiltration and is a potential therapeutic target. *J Clin Invest*. 2019;129(1):137-149.

doi: 10.1172/JCI121266

41. Wei C, Wang B, Peng D, *et al*. Pan-cancer analysis shows that ALKBH5 is a potential prognostic and immunotherapeutic biomarker for multiple cancer types including gliomas. *Front Immunol*. 2022;13:849592.

doi: 10.3389/fimmu.2022.849592

42. Liu L, Zhang X, Ding H, *et al*. Arginine and lysine methylation of MRPS23 promotes breast cancer metastasis through regulating OXPHOS. *Oncogene*. 2021;40(20):3548-3563.

doi: 10.1038/s41388-021-01785-7

43. Oviya RP, Thangaretnam KP, Ramachandran B, *et al*. Mitochondrial ribosomal small subunit (MRPS) MRPS23 protein-protein interaction reveals phosphorylation by CDK11-p58 affecting cell proliferation and knockdown of MRPS23 sensitizes breast cancer cells to CDK1 inhibitors. *Mol Biol Rep*. 2022;49(10):9521-9534.

doi: 10.1007/s11033-022-07842-y

44. Wang Q, Chen G, Liu L, *et al*. MRPS23 is a novel prognostic biomarker and promotes glioma progression. *Aging (Albany NY)*. 2024;16(3):2457-2474.

doi: 10.18632/aging.205493

45. Weller M, Wen PY, Chang SM, *et al*. Glioma. *Nat Rev Dis Primers*. 2024;10(1):33.

doi: 10.1038/s41572-024-00516-y