High expression of COPB2 predicts adverse outcomes: A potential therapeutic target for glioma

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Abstract
Aims: To evaluate the clinical significance of coatomer protein complex subunit beta 2 (COPB2) in patients with glioma using a bioinformatics analysis.

Methods: Oncomine, GEO, and The Cancer Genome Atlas databases were used to examine the COPB2 transcript levels in glioma tissues. Gene expression profiles with clinical information from low-grade glioma and glioblastoma (GBM) projects were analyzed for associations between COPB2 expression and clinicopathologic characteristics. Kaplan-Meier survival and Cox regression analyses were used for survival analysis. Gene set enrichment analysis (GSEA) was conducted to screen the pathways involved in COPB2 expression. Gene set variation analysis (GSVA) and correlation analysis were performed to verify the correlations between COPB2 and inflammatory responses. Canonical correlation analyses examined whether COPB2-high patients have more infiltrating inflammatory and immune cells.

Results: COPB2 was highly expressed in gliomas and high COPB2 expression correlated with shorter overall survival time and several poor clinical prognostic variables. GSEA indicated that some immune-related pathways and other signaling pathways in cancer were associated with the COPB2-high phenotype. The GSVA and canonical correlation analysis demonstrated that COPB2 expression was closely linked to inflammatory and immune responses, and higher immune cell infiltration.

Conclusions: COPB2 may be a potential prognostic biomarker and an immunotherapeutic target for glioma.

KEYWORDS
biomarker, COPB2, gene set enrichment analysis, gene set variation analysis, glioma

1 | INTRODUCTION

Gliomas are the most common malignant brain tumors with high recurrence and lethality rates.1 According to the classification of the World Health Organization (WHO), brain gliomas are categorized into four grades (I-IV).2 Glioblastoma multiforme (GBM, grade IV) exhibits a malignant phenotype associated with high proliferative activity, potent invasive ability, and vascular formation with a median survival rate of no more than 15 months postdiagnosis.3 With the development of biomedical techniques, several biomarkers and
molecular classifications of glioma have been established. However, effective and reliable biomarkers that could predict poor prognosis and direct treatment strategies are rare. Thus, the identification of efficient neuropathological biomarkers and therapeutic targets is urgently required.

The coatomer protein complex subunit beta 2 (COPB2), also known as beta prime-COP or beta-Cop, is one of the seven subunits that form coatomer complex I. COPB2 serves as a mediator in the process of protein synthesis which transports proteins from the endoplasmic reticulum (ER) to the Golgi apparatus. Recently, COPB2 has been viewed as a new oncogene in many cancer types. Bhandari et al. reported that the upregulation of COPB2 in breast cancer is associated with age and lymph node metastasis in a validated cohort and promotes tumor cell proliferation and invasion. Further, a recent study demonstrated that COPB2 could be a potential target gene in prostate cancer. Loss of function experiments demonstrated that COPB2 downregulation arrests the cell cycle at G1 and G2 phases and induces cell apoptosis. Pu et al. reported that COPB2 upregulation in lung adenocarcinoma cell lines facilitates cell growth and tumorigenesis via upregulating YAP1 expression. These previous findings indicated that COPB2 might play a critical role in the development of cancer. Yet, the clinical significance of COPB2 in glioma remains unclear.

Thus, this research aimed to reveal the association between COPB2 and glioma and explore the potential prognostic value of COPB2 in patients with glioma based on The Cancer Genome Atlas (TCGA), Oncomine, and the Gene Expression Omnibus (GEO) databases. The results indicated that COPB2 was significantly overexpressed in glioma tissues compared with nontumor tissues and that higher COPB2 expression was correlated with higher WHO grade, shorter overall survival (OS) time, and several poor clinical prognostic variables. Gene set enrichment analysis (GSEA) showed that some immune-related pathways and other signaling pathways in cancer were associated with the COPB2 high expression phenotype, shedding light on the molecular mechanisms underlying the onset and progression of glioma. Gene set variation analysis (GSVA) and canonical correlation analysis demonstrated COPB2 expression was closely linked to a higher infiltration of immune cells, as well as inflammatory and immune responses.

2 | METHODS

2.1 | Public database and bioinformatics analysis

The transcript level of COPB2 in different cancers was ascertained by the Oncomine database (https://www.oncomine.org/resource/main.html), with a threshold set as such—top gene rank 10%, fold change >2, and P-value <1E-4. The microarray data of patients with glioma were downloaded from the GEO (https://www.ncbi.nlm.nih.gov/geo) public database under accession number GSE16011. Gene expression profile data containing clinical information from low-grade glioma and GBM projects (HTSeq-FPKM) were obtained from TCGA database (http://cancergenome.nih.gov/). The data from TCGA were further analyzed for associations between COPB2 expression and clinicopathologic characteristics in glioma.
2.2 | Gene set enrichment analysis and gene set variation analysis

To investigate the potential mechanisms underlying the interaction of COPB2 expression on glioma progression, a GSEA was conducted to screen out whether some biological pathways showed statistically significant differences between high and low COPB2 expression groups. For each analysis, gene set permutations were implemented 1000 times. Gene sets with a false discovery rate (FDR) <0.05 and normal P-value <.05 were viewed as significantly enriched. Moreover, GSVA was performed to transform gene expression values into scores for inflammatory response metagene sets, followed by the application of correlograms to further verify correlations between COPB2 and these metagenes.

3 | RESULTS

3.1 | Glioma COPB2 transcript levels in different databases

Firstly, the transcript levels of COPB2 in different cancers were analyzed. The Oncomine database (one of the main functions of which is gene expression differential analysis) was used to explore the expression of COPB2 mRNA in different cancers (Figure 1A), and 189 datasets, including 33,144 samples, were included. Relative to normal clinical specimens, COPB2 indicated significant hyperexpression in bladder, brain and central nervous system, breast, esophageal, head and neck, lung, lymphoma, sarcoma, and other cancers, but hyporepressed in leukemia (Figure 1A), suggesting that the high expression of COPB2 is common in various types of cancer. The detailed expression profile was summarized in Table S1.

In glioma, 675 glioma patients with COPB2 expression profile data were obtained from TCGA COPB2 is significantly upregulated in tumor tissues relative to nontumor tissues (Figure 1B, P < .001). In addition, we also used the GSE16011 dataset from GEO database for the purpose of validation (Figure 1C, P < .001). The results indicated increased transcript levels of COPB2 in glioma.

3.2 | TCGA glioma patient characteristics

As the TCGA database contains sufficient glioma samples, we only selected this database for further analysis of the association between gene and clinical characteristics. A total of 1114 cases (Table 1) with both gene expression and clinical data were available for 194 astrocytomas, 191 oligodendrogliomas, 130 oligoastrocytomas, 596 GBMs, and three cases that lacked histological information. The median age of patients was 52 years old, and there were 651 men and 460 women. The study cohort included 249 grade II, 265 grade III, and 596 grade IV cases, but unfortunately did not include any grade I cases. Only 125 cases were tested for the IDH1 mutation—8.17% (n = 91) were classified as a mutated type while 3.05% (n = 34) were not. With respect to KPS (Karnofsky Performance Score), 52.4% (n = 584) patients scored ≥80 points and 13.6% (n = 151) were <80.

### Table 1: The Cancer Genome Atlas glioma patient characteristics

| Clinical characteristics | No. of patients | Percentage (%) |
|--------------------------|-----------------|----------------|
| Age (y) 9-89              | Median 52       |                |
| Sex                       |                 |                |
| Male                      | 651             | 58.4           |
| Female                    | 460             | 41.3           |
| Missing                   | 3               | 0.270          |
| Vital status              |                 |                |
| Alive                     | 570             | 51.2           |
| Dead                      | 539             | 48.4           |
| Missing                   | 5               | 0.450          |
| WHO grade                 |                 |                |
| G2                        | 249             | 22.4           |
| G3                        | 265             | 23.8           |
| G4                        | 596             | 53.5           |
| Missing                   | 4               | 3.60           |
| Histology                 |                 |                |
| Astrocytoma               | 194             | 17.4           |
| Oligodendroglioma         | 191             | 17.2           |
| Oligoastrocytoma          | 130             | 11.7           |
| Glioblastoma              | 596             | 53.5           |
| Missing                   | 3               | 0.270          |
| KPS                       |                 |                |
| <80                       | 151             | 13.6           |
| ≥80                       | 584             | 52.4           |
| Missing                   | 379             | 34.0           |
| Tumor status              |                 |                |
| Tumor-free                | 209             | 18.8           |
| With tumor                | 783             | 70.3           |
| Missing                   | 122             | 11.0           |
| IDH1 mutation             |                 |                |
| Yes                       | 91              | 8.17           |
| No                        | 34              | 3.05           |
| Missing                   | 989             | 88.8           |
| Family history of cancer  |                 |                |
| Yes                       | 132             | 11.9           |
| No                        | 210             | 18.9           |
| Missing                   | 772             | 69.3           |
| Ethnicity                 |                 |                |
| Hispanic or Latino        | 45              | 4.04           |
| Not Hispanic or Latino    | 939             | 84.3           |
| Missing                   | 130             | 11.7           |

2.3 | Statistical analysis

The statistical analyses were performed utilizing R software v3.5.1. Descriptive statistics were used to summarize the molecular and clinical characteristics of patients in the TCGA database. To analyze potential relationships between COPB2 and clinicopathologic features, Mann-Whitney U and logistic regression tests were used. The Kaplan-Meier method and Cox regression analyses were used to compare the impact of COPB2 expression on the OS of TCGA patients alongside with other clinical variables. The remaining correlations between COPB2 expression and inflammatory and immune cell types were detected by using canonical correlation analysis in GraphPad Prism 7 and SPSS 25.0. In all statistical analyses conducted, a P-value <.05 was viewed as statistically significant.
points. There were 209 tumor-free (18.8%) and 783 tumor (70.3%) patients. A family history of cancer was present in 132 cases (11.9%). In respect to ethnicity, 4.04% (n = 45) were Hispanic or Latino, while the majority of cases (84.3%, n = 939) were not Hispanic or Latino. Finally, 51.7% (n = 570) patients were alive at last follow-up contact and 48.4% (n = 539) were dead, while five patients lost contact.

### 3.3 Association with COPB2 expression and clinicopathologic features

To explore the expression pattern of COPB2 in gliomas, mRNA expression profiles from the TCGA database were obtained and analyzed. As shown in Figure 2(A-H), increased expression of COPB2 correlated significantly with tumor grade ($P < .001$), histological type ($P < .001$), age ($P < .001$), KPS ($P = .0260$), tumor status ($P < .001$), and vital status ($P < .001$). Despite the lack of significant differences, a correlated trend was observed for IDH1 mutation ($P = .114$) and family history of cancer ($P = .219$).

Univariate analysis using logistic regression revealed that COPB2 expression (ground on median expression value) was linked to poor prognostic clinicopathologic variables (Table 2). Increased COPB2 expression in glioma was significantly associated with age ($\geq 52$ vs $< 52$, OR = 2.35, 95%CI [1.71-3.23], $P < .001$), vital status (dead vs alive, OR = 2.89, 95%CI [2.07-4.07], $P < .001$), grade (III vs II, OR = 1.92, 95%CI [1.35-2.76], $P < .001$; IV vs II, OR = 8.00, 95%CI [5.07-12.9], $P < .001$), histology type (GBM vs astrocytoma, OR = 4.20, 95%CI [2.70-6.61], $P < .001$; GBM vs oligoastrocytoma, OR = 6.08, 95%CI [3.67-10.3], $P < .001$; and GBM vs oligodendroglioma, OR = 5.54, 95%CI [3.52-8.85], $P < .001$), tumor status (with tumor vs tumor-free, OR = 3.11, 95%CI [2.17-4.50], $P < .001$), and KPS ($< 80$ vs $\geq 80$, OR = 1.80, 95%CI [1.07-3.07], $P = .03$). No significant differences were found on the sex, IDH1 mutation, ethnicity,
TABLE 2 COPB2 expression associated with clinical-pathological characteristics (logistic regression)

| Clinical characteristics                  | Total (N) | Odds ratio in COPB2 expression | P-value |
|-------------------------------------------|-----------|---------------------------------|---------|
| Age (≥52 vs <52)                          | 670       | 2.35 (1.71-3.23)                | <.001   |
| Sex (male vs female)                      | 670       | 1.10 (0.81-1.50)                | .530    |
| Vital status (dead vs alive)              | 670       | 2.89 (2.07-4.07)                | <.001   |
| Grade (III vs II)                         | 509       | 1.92 (1.35-2.76)                | <.001   |
| (IV vs II)                                | 409       | 8.00 (5.07-12.89)               | <.001   |
| Histological type                         |           |                                 |         |
| (GBM vs astrocytoma)                      | 352       | 4.20 (2.70-6.61)                | <.001   |
| (GBM vs oligoastrocytoma)                 | 288       | 6.08 (3.67-10.29)               | <.001   |
| (GBM vs oligodendroglioma)                | 350       | 5.54 (3.52-8.85)                | <.001   |
| Tumor status (with tumor vs tumor-free)   | 591       | 3.11 (2.17-4.50)                | <.001   |
| IDH1 mutation (yes vs no)                 | 126       | 0.510 (0.220-1.12)              | .100    |
| KPS (<80 vs ≥80)                          | 413       | 1.80 (1.07-3.07)                | .0300   |
| Ethnicity (Hispanic or Latino vs not      | 609       | 1.28 (0.640-2.61)               | .490    |
| Family history of cancer (yes vs no)      | 338       | 1.22 (0.790-1.89)               | .370    |

and family history of cancer subgroups. These results essentially indicate that COPB2 may serve as an oncogene and glioma patients with high COPB2 expression are liable to progress to a more advanced WHO grades, worse histology types, and gain lower KPS points.

3.4 Survival outcomes and multivariate analysis

To investigate the predictive implications of COPB2 in glioma prognosis, we analyzed COPB2 expression and the OS in the TCGA database. After eliminating patients with absent OS data, remaining patients underwent a Kaplan-Meier analysis. Glioma patients with COPB2-high had a worse prognosis than that with COPB2-low (Figure 2I, P < .001).

Univariate and multivariate Cox analyses were conducted to further explore the prognostic value of COPB2. In total, 342 gliomas patients with integrated data containing all the variables were analyzed. The univariate Cox regression revealed that COPB2-high correlated significantly with a worse OS (hazard ratio [HR]: 3.70, 95%CI [2.52-5.44], P < .001) (Table 3). Other clinicopathologic characteristics associated with poor survival were age (HR = 3.70, 95%CI [2.52-5.44]), WHO grade (HR = 5.32, 95%CI [3.88-7.31]), histological type (HR = 1.89, 95%CI [1.54-2.30]), KPS (HR = 2.26, 95%CI [1.41-3.62]), and tumor status (HR = 39.7, 95%CI [5.53-284]), all with

### TABLE 3 (A) Univariate analysis of clinicopathologic characteristics and overall survival in The Cancer Genome Atlas cohort. (B) Multivariate analysis postvariable selection

| Characteristics | Hazard ratio (95% CI) | P-value |
|-----------------|-----------------------|---------|
| A.              |                       |         |
| Age             | 3.70 (2.52-5.44)       | <.001   |
| Gender          | 1.08 (0.750-1.55)      | .696    |
| Grade           | 5.32 (3.88-7.31)       | <.001   |
| Histological type| 1.89 (1.54-2.30)       | <.001   |
| KPS             | 2.26 (1.41-3.62)       | <.001   |
| Tumor status    | 39.7 (5.53-284)        | <.001   |
| Ethnicity       | 0.480 (0.150-1.51)     | .209    |
| COPB2 expression| 1.13 (1.09-1.18)       | <.001   |
| B.              |                       |         |
| Tumor status    | 4.51 (3.29-6.18)       | <.001   |
| Histological type| 1.07 (0.900-1.27)      | .452    |
| COPB2 expression| 1.05 (1.01-1.08)       | .00600  |

P < .001. The multivariate Cox analysis identified COPB2 remained independently associated with OS, with a HR of 1.05 (CI: 1.01-1.08, P = .006), along with tumor status.

3.5 COPB2-related signaling pathways based on GSEA

As many signaling pathways contribute to tumor initiation and progression, the poor prognosis of COPB2-high may be related to the numerous signaling pathways activated in glioma. GSEA was utilized to recognize signaling pathways involved in glioma between low and high COPB2 expression cohorts. Significant differences (normalized P < .05, FDR < 0.05) were observed in the enrichment of the MSigDB Collection (kegg.v6.2.symbols.gmt).

Several signaling pathways—especially inflammation- and immunity-related pathways—were enriched in the COPB2 high expression phenotype, including B-cell receptor, T-cell receptor, natural killer (NK) cell-mediated cytotoxicity, antigen processing and presentation, Fc gamma R-mediated phagocytosis, cytokine-cytokine receptor interaction, leukocyte transendothelial migration, and other pathways in cancer (please see Figure 3 and Table 4).

3.6 COPB2-related inflammatory response

To better comprehend COPB2-related inflammatory activities, seven immune system-related metagene clusters (comprising 104 genes) that serve as surrogate markers of different immunological cell types were employed (Data S1). COPB2 expression, metagenes expression, age, gender, vital status, tumor grade, and histology of samples were displayed on a heat map in Figure 4. COPB2 expression was positively correlated with most genes of the gene sets HCK, LCK, interferon, STAT1, MHC I, and MHC II, but
negatively with most IgG genes. To validate the heatmap analysis, a GSVA was conducted to transform gene expression values into enrichment scores for each metagene set. Correlograms were generated (using the R language program) to measure correlations between COPB2 expression and the enrichment scores of the seven metagenes—these confirmed the aforementioned results (Figure 5A).

### 3.7 Relationship between COPB2 and infiltrating immune cells

Previous studies reported that tumor-infiltrating immune cells may represent a crucial pathophysiological factor in the onset and progression of glioma.15 We examined the relationship between COPB2 and six immune cell types that frequently infiltrate the tumor microenvironment, including innate immune cells: neutrophils, tumor-associated macrophages (TAMs), NK cells, and myeloid-derived suppressor cells (MDSCs)16,17 and adaptive immune cells: CD8+ T cells and regulatory T cells (Tregs).18,19 The specific biomarker genes of each immune cell type are displayed in Data S2. Canonical correlation analysis revealed that the transcript levels of COPB2 were positively correlated with the marker gene expression of these six immune cell types in the TCGA datasets (Figure 5B, P < .001), indicating that glioma patients with COPB2-high were prone to have more immune cells infiltrated than glioma patients with COPB2-low.

### 4 DISCUSSION

In our study, the quantitative results indicated that COPB2 had higher expression levels in most cancers compared with normal tissues in the Oncomine database. In addition, COPB2’s high expression in patients with glioma was further validated in the TCGA and GEO databases. RNA sequencing data from TCGA were also obtained and analyzed. COPB2 expression levels were correlated

#### TABLE 4 Gene sets enriched in high COPB2 expression phenotype

| MSigDB collection               | Gene set name                                      | NES  | NOM P-value | FDR q-value |
|---------------------------------|----------------------------------------------------|------|-------------|-------------|
| Kegg.v6.2.symbols.gmt           | KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION          | 1.78 | .0180       | 0.0250      |
|                                 | KEGG_B_CELL_RECEPTOR_SIGNALING_PATHWAY            | 1.73 | .0240       | 0.0300      |
|                                 | KEGG_T_CELL_RECEPTOR_SIGNALING_PATHWAY            | 1.68 | .0250       | 0.0390      |
|                                 | KEGG_FC_GAMMA_R_MEDIATED_PHAGOCYTOSIS             | 1.80 | .00800      | 0.0220      |
|                                 | KEGG_NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY    | 1.66 | .0330       | 0.0420      |
|                                 | KEGG_LEUKOCYTE_TRANSENDOTHelial_MIGRATION         | 1.91 | .00200      | 0.0110      |
|                                 | KEGG_PATHWAYS_IN_CANCER                           | 2.14 | 0           | 0.00300     |
|                                 | KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION       | 1.73 | .0270       | 0.0300      |

Note: Gene sets with NOM P-value <.05 and FDR q-value <0.05 were considered as significantly enriched. Abbreviations: FDR, false discovery rate; NES, normalized enrichment score; NOM, nominal.
FIGURE 4 COPB2-related inflammatory response. Heat maps displaying COPB2 expression, the clinicopathological parameters, and seven well-established metagenes from the TCGA datasets.
with advanced clinicopathological parameters (high grade, histological type, tumor status, age, vital status, and KPS) and a shorter survival time. Univariate and multivariate Cox analyses showed that \( \text{COPB2} \) may be a promising biomarker for glioma prognosis while a GSEA using TCGA data revealed that some inflammation- and immunity-related pathways and other signaling pathways in cancer are differentially enriched in the \( \text{COPB2} \) high expression phenotype. To further investigate \( \text{COPB2} \)-related inflammatory activities, heatmaps using seven immune-related metagenes demonstrated that \( \text{COPB2} \) transcript levels were positively correlated with gene sets for \( \text{HCK} \), \( \text{LCK} \), interferon, \( \text{STAT1} \), \( \text{MHC I} \), and \( \text{MHC II} \) but negatively with IgG, a marker basically associated with B cells. These results were verified by correlograms analysis using GSVA. Moreover, a positive correlation was observed between \( \text{COPB2} \) and...
et al.23 reported that macrophages/glioma‐associated microglia evade immune system surveillance (Table 5). For example, Roesch also transform said cells into phenotypes that can help tumor cells.

COPB2 explore the interaction between laboratory research and clinical trials are required to exhaustively adverse clinical outcomes in patients with cancer. However, future which might exhibit immunosuppressive activities and leading to cell types—such as Tregs, neutrophils, and MDSCs (Figure 5B)—COPB2 transcript levels and immunosuppressive relation between immune microenvironment of glioma. Here, we observed a cor ‐ discovery of the present study is that COPB2 was involved in the process of disease progression.20 Recently, some reports found significant differences in COPB2’s expression in various tumors. Underexpression of COPB2 could downregulate the EMT‐related protein N‐cadherin and vimentin which may promote breast tumor cell invasion.6 Knockdown of COPB2 led to cell apoptosis by inhibiting the RTK signaling cascade molecules in gastric cancer.21 In lung adenocarcinoma,7 patients with COPB2-high had worse survival status than COPB2-low. In the present study, we demonstrated that the overexpression of COPB2 in glioma was correlated with advanced clinicopathologic characteristics and predicts worse outcomes. These findings indicated that COPB2 may be regarded as a promising target for cancer gene therapy.

Glioma cells could release multiple cytokines that promote the infiltration of various immune cells such as MDSCs, microglia, Tregs, macrophages, CD8 T cells, and CD4 T cells into the tumor microenvironment,22 as tumors not only recruit immune cells, but also transform said cells into phenotypes that can help tumor cells evade immune system surveillance (Table 5). For example, Roesch et al.23 reported that macrophages/glioma‐associated microglia (GAMs) tend to gather in tumor sites and generate an immunosuppressive tumor microenvironment which promote glioma invasion, growth, and angiogenesis.22,24 Interestingly, one novel discovery of the present study is that COPB2 was involved in the immune microenvironment of glioma. Here, we observed a correlation between COPB2 transcript levels and immunosuppressive cell types—such as Tregs, neutrophils, and MDSCs (Figure 5B)—which might exhibit immunosuppressive activities and leading to adverse clinical outcomes in patients with cancer. However, future laboratory research and clinical trials are required to exhaustively explore the interaction between COPB2 and immunosuppressive cells.

In recent years, the use of immune checkpoint inhibitors (ICIs) has been popular in the treatment of malignant tumors.25,26 Some ICIs, such as anti‐PD‐1 antibody, are superior to traditional chemo‐radiotherapy in terms of its clinical curative effect.27 However, certain types of malignant tumors, such as glioblastoma, are resistant to monotherapy with ICIs.27,28 Therefore, new immunotherapeutic targets are urgently needed to treat glioma. Bullock BL et al.29 demonstrated that IFN‐γ signaling represents an important pathway in the resistance to anti‐PD‐1 treatment in cancer. In the present study, COPB2 expression was observed to be positively associated with the interferon gene sets (Figures 4 and 5A). Thus, it makes sense to try to combine anti‐PD‐1 therapy and anti‐COPB2 therapy to amplify the efficacy of treatments typically used in isolation.

Some limitations were present in this study: First, the number of patients incorporated in the univariate and multivariate Cox analyses patients were reduced as many patients had missing integrated data on all variables; second, only a small number of healthy samples were used as controls, so additional studies are needed to balance sample size; and lastly, laboratory studies should be carried out to elucidate the precise mechanisms of COPB2 overexpression in human glioma and clarify its relationship with poor prognosis and immunomodulation.

5  |  CONCLUSION

As far as we are aware, at present, this is the first study to explore the prognostic value of COPB2 in patients with glioma. This study revealed that COPB2 expression was upregulated in glioma samples and was related to adverse outcomes. We also found that COPB2 may represent an important factor in the immunomodulation of the glioma immune microenvironment. Therefore, taken together, COPB2 may act as a potential biomarker of prognosis and immunotherapeutic target for glioma.

CONFLICT OF INTEREST

The authors declare no conflict of interest.
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