Proteomics-based prognostic signature predicts prognosis and immunity in glioma

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Abstract

The prognosis of glioma patients is closely associated with the expression of immune cells and oncoproteins. Therefore, protein-related signatures were conducted to improve the prediction of overall survival (OS) in glioma patients after surgery. Differential oncoproteins were selected from the Renji cohort and The Cancer Genome Atlas (TCGA) database. The least absolute shrinkage and selection operator (LASSO) regression model is designed to construct the multiple oncoprotein model related to OS in two test series. Furthermore, the 6-oncoprotein model was tight associated with immune cell infiltration, immune function, and immunotherapy. In summary, the 6-oncoprotein marker, a favorable biomarker for the prognosis and immune characteristics of glioma, could help individualized immunotherapy for patients with glioma.

Introduction

Glioma is an important cause of cancer-related death, constituting more than 40% of all primary CNS neoplasms. However, less than 60% of patients survive 5 years with chemoradiotherapy or surgical resection, especially since the median survival time for glioblastoma(GBM) patients is still merely 12–14 months (1). In the past decade, targeted therapy and immunotherapy have been widely used to improve patients' prognosis after surgery(2, 3). Therefore, the prognostic biomarkers and immunotherapy of gliomas are increasingly worth exploring.

Proteomics is parallel to the genomic and metabolomic analyses and unifies proteomics-based signaling into signaling networks (4–8). Proteins can control cellular transformation processes, and genomics functionally, which could supplement new insights into the mechanisms of malignant transformation. It is important to note that changes in DNA or transcript levels or abundance correlate poorly with the abundance of protein; therefore, proteomics bridges the gap between functional proteins and genomic information, and also, translates this information(9). Proteomic approaches could identify new biomarkers for the glioma prognosis. Indeed, mRNA, IncRNA, or circRNA can be biomarkers for predicting glioma survival time in many studies(10–12), however, dysregulation of mRNA expression in gliomas does not equate to corresponding protein products as tumor markers, because mRNA expression is poorly correlated with protein levels(13). Even if the VEGF and some angiogenesis-related proteins, extracellular matrix proteins, matrix metalloproteinases, glial fibrillary acidic protein (GFAP), macrophage migration inhibitory factor (MIF), and function-associated proteins are made to glioblastoma protein markers in several studies (14), single protein exhibit markedly insufficient specificity and sensitivity. Therefore, in our studies, we establish a multi-oncoprotein signature for predicting the OS of glioma patients after surgery.

Immunotherapy has attracted more and more attention for the therapy of glioma, and the immune surrounding of glioma determines the effect of immunotherapy. Because of the blood-brain barrier (BBB, which consists of astrocytes, pericytes, and endothelial cells), most peripheral immune cells have trouble getting into the brain; however, tumors secrete high levels of soluble factors such as VEGF and matrix
metalloproteinases (MMPs), which could damage endothelial junctions, leading to the infiltration of various immune cells(15). Microglia can regulate the growth of glioma by promoting its proliferation, invasion, and stemness(16–19). Anti-inflammatory macrophages (AIM) mediate glioma recurrence by promoting angiogenesis and interacting with microglia to promote tumorigenesis(20–22). Thus, we perform a risk model for Individualized immunotherapy for glioma patients.

In the research, we made attempts to establish a proteomic-based multi-marker signature to improve the outcome of glioma and offer credible strategies to guide individual immunological therapy. Glioma samples were obtained from the Renji cohort and TCGA database, and the Least absolute shrinkage and selection operator (LASSO) regression model was used to predict the OS of glioma patients with multi-protein index. The ability of the model was verified in the TCGA-train subgroup, TCGA-test subgroup, and Renji cohort. Besides, the 6-protein signature was tight associated with immune characteristics and immunotherapy of glioma. These results may provide an effective method for the prognosis prediction of individualized immunotherapy in patients with glioma.

**Materials And Methods**

**Preparations of glioma Clinical Specimens and Common database**

Proteome profiling data, transcriptome profiling, and clinical data of glioma were downloaded from The Cancer Genome Atlas (TCGA) database.

Clinical samples of glioma were collected from the neurosurgery department, Ren Ji Hospital, Shanghai Jiaotong University between June 1, 2018, and July 1, 2022. The research was carried out according to the Declaration of Helsinki. Ethical principles for Biomedical Research involving Human Subjects Shanghai Jiaotong University School of Medicine, Renji Hospital Ethics Committee (Ethics Committee No. RA-2021-046) approved the study and waived the need for informed consent in accordance with the Regulation of the People's Republic of China on the Administration of Human Genetic Resources. Finally, 14 patients' glioma tissues were obtained, and 4 non-tumor brain tissues from epileptic foci of epilepsy. Follow-up information for these glioma patients was obtained every 2–3 months and every 3–6 months for the first 2 years until July 30, 2022. The OS was counted from the date of the surgical removal of the tumor until the last follow-up visit or death. However, two patients lost to follow-up, the clinical information was collected in Table S1.

**Construction Of The LASSO Regression Model**

For these differentially expressed 46 proteins were statistically identified in univariate Cox regression and then proteins associated with prognosis were selected for further analysis. Through these proteins, we established LASSO COX regression models using the R package "glmnet". Based on the highest lambda
value that was selected through 1,000 cross-validations in the Lasso method (lambda. min), a series of prognostic proteins and their LASSO coefficients were achieved. Based on the coefficient, the TCGA cohort was divided into low-risk and high-risk subgroups according to the median risk scores. The protein risk model of OS was counted by multiplying the corresponding coefficient and the expression level of each glioma protein.

**Quantitative Analysis Of Proteomics**

The parallel reaction monitoring technique (PRM) possessed high resolution and trapping capabilities of the instrument, which is generally operated on the latest generation HRAM hybrid instruments, namely the quadrupole time-of-flight (Q-TOF) and the quadrupole-Orbitrap mass spectrometers. The 18 samples were collected and stored in a -80 Celsius refrigerator. Next, the quantitative analysis of proteomics was performed in the Luming corporation. Finally, the protein quantitation data was shown in Table S2.

**Statistical analysis**

TIDE score between low-risk and high-risk subgroups was compared by the Wilcoxon test. OS between the two risk subgroups was evaluated by Kaplan–Meier (KM) survival and univariate survival analysis, which were compared via the Cox regression and log-rank test, respectively. The R package “pROC” was used to perform Time-dependent ROC curves. The difference was statistically significant at P < 0.05.

**Results**

**Identification of differentially expressed proteins and functional analysis in glioma samples from the Renji cohort**

The standardization of glioma samples was shown in Supplementary Figs. 1, and ASD and samples tree were shown in Supplementary Figs. 1A-B. Next, normalized protein expression and original protein expression of glioma were shown in Supplementary Figs. 1C-D, respectively. Besides, normalized protein density and original protein density were performed in Supplementary Figs. 1E-F, respectively. Finally, the data on protein expression was Proteome profiling data collected in Table S2.

The functional analysis of those proteins was performed in Fig. 1. Biological processes (BP), molecular function (MF), and cellular component (CC) were shown in Fig. 1A, and KEGG pathway analysis was shown in Fig. 1B. Then, a heatmap between tumor specimens and non-tumor specimens was performed in Fig. 1C. As shown in Fig. 1D, differentially expressed proteins were selected, which consisted of 1512 up-regulated proteins and 1101 down-regulated proteins. Finally, KEGG pathway classification between up and down-regulated proteins was shown in Fig. 1E, upregulated proteins mostly participated in environmental information processing and organismal systems, however, most downregulated proteins were involved in signal transduction and endocrine system.
Furthermore, BP, CC, and MF of downregulated proteins were shown in Supplementary Figs. 2A, and the KEGG pathway was shown in Supplementary Figs. 2C. At the same time, functional and KEGG pathways of upregulated proteins were performed in Supplementary Figs. 2B and D, respectively. Besides, PPI genes and PPI query of these glioma proteins were shown in Supplementary Figs. 2E-F.

Establishment of a 6-protein signature from the TCGA database.

The proteomic analysis and clinical data of glioma were collected from the TCGA database, after combining proteome profiling data and overall survival, 456 proteins from the TCGA database remained. Further overlapping analysis was performed between TCGA and Renji group, in which 42 proteins were obtained and were believed to be commonly differential expression in glioma (Supplementary Figs. 3). Next, the "glmnet" software package was performed to establish the glioma prognosis prediction risk model, and the model sequence was returned for 10-fold cross-validation to pick out the optimization model. Then, the Lambda of the risk score model was performed in Fig. 2A. After 10 times of cross-validation, the operation to 100 times, and calculating the average value of cross-validation errors, the 6 proteins were selected to construct the prognostic risk model (Fig. 2B). Eventually, the risk scoring of each protein and specimen was collected in Table S3 and Table S4, respectively.

Verification Of The 6-protein Signature In Predicting Prognosis Of Glioma

Specimens chosen from the TCGA database were randomly assigned to train and test subgroups. In the training group, the high-risk score subgroup had a worse prognosis than the low-risk score subgroup (log-test p < 0.001, Fig. 3A), besides, all glioma patients were divided into low-risk and high-risk subgroups according to the median risk score as the cut-off value (Fig. 3C), as well as, an overview of the survival state and risk score was shown in Fig. 3E. Meanwhile, K-M survival analysis revealed that low-risk score patients had a better prognosis after surgery in the test subgroup (log-test p < 0.001, Fig. 3B), As shown in Fig. 3D, F, as the risk score increased, more glioma patients dead.

Furthermore, the risk model performed a superior prediction value in all TCGA samples (Supplementary Figs. 4). As shown in the heatmap, VAV1, IGFBP2, COG3, MSH2, and BAX were upregulated in the high-risk subgroup, however, SOX2 was over-expression in the low-risk group (Supplementary Figs. 4A). Then, Risk score curves, Dot diagrams, and K-M survival curves indicated that the 6-protein signature had predicted glioma patients’ prognosis after surgery perfectly (log-test p < 0.001, Supplementary Figs. 4B-D). Compared to age and gender, the risk model had more accurate forecasting capabilities (Supplementary Figs. 4E), meanwhile, the 6-protein signature and OS in the time-dependent ROC curves were 0.822 for 1 year, 0.890 for 3 years, and 0.866 for 5 years (Supplementary Figs. 4F). According to cluster analysis, those TCGA glioma samples divide into three parts (C1, C2, and C3), and C2 had a minimum survival time compared to C1 and C3 (log-test p < 0.001, Supplementary Figs. 4G-H).
Besides, we found that six proteins in the risk model also had better prediction values in OS of glioma patients. As demonstrated in Figure S5, the K-M survival curve indicates that every protein could distinguish the different prognostic statuses (log-test p < 0.001, Supplementary Figs. 5).

To further confirm whether the 6-protein classifier owns a similar predictive power in different clinical centers, we performed it at the Renji Hospital clinical center. The risk model and OS in the time-dependent ROC curves were 1.000 for 0.5-year, 1.000 for 0.75-year, and 0.907 for 1-year (Supplementary Figs. 6A). Furthermore, the AUC of the 6-protein signature was observably greater than gender or age at 0.5-year, 0.75-year, and 1 year (Supplementary Figs. 6B-D).

The Correlation Between 6-protein Signature And Immune Cells

The expression of 26 kinds of immune cells including CD4+ T cells, CD8+ T cells, Treg, NK cells, and plasma cells was collected through the CIBERSORT database. The expression of B cell naïve, Macrophage M0, Macrophage M1, Macrophage M2, T cells regulatory, T cells CD8, as well as were T cells follicular helper lower in the low-risk subgroup (p < 0.05, Fig. 4A-H), however, NK cells activated was lower in the high-risk subgroup (p < 0.05, Fig. 4I). Meanwhile, the expression of eosinophils, Mast cells activated and Monocytes was higher in the low-risk subgroup (p < 0.05, Supplementary Figs. 7A-C), while, in the high-risk subgroup, the expression of Mast cells resting was higher (p < 0.05, Supplementary Figs. 7D). Besides, differential expression of all immune cells between high and low risk groups was performed in Supplementary Figs. 7E.

Furthermore, K-M survival analysis indicated that abundant B cells naïve, Neutrophils, Macrophage M0, Macrophage M1, Macrophage M2, NK cells resting, T cells follicular helper, and T cells regulatory had more tendency to recurrence (Fig. 5A-H). While abundant NK cells activated, Mast cells activated, Monocytes, and Eosinophils had a longer overall survival time (Fig. 5I-L).

Immune Characteristics Of The Two 6-protein Signature Subgroups

The KM survival curves showed that CD8+ T cells, B cells, T cell co-inhibition, T cell co-stimulation, T helper cells, Tfh, Th1 cells, and other immune-related function activities could foresee the OS of glioma patients. The more active the immune-related function, the shorter the survival time (p < 0.05, Figs. 6A–L). Cells associated with immune function, such as B cells, T-helper cells, and mast cells were observably inhibited in the low-risk subgroup (p < 0.05, Supplementary Figs. 8). All the immune function were collected in Supplementary Fig. 9, unfortunately, DCs was not the difference between the two subgroups.

The 6-protein Signature Predicted Immunotherapy

The expression (CD274) of PD-L1 was suppressed in the low-risk subgroup compared with the high-risk subgroup (Fig. 7A), and PD-L1 had positively associated with risk score (Fig. 7B). TIDE was used to
evaluate the potential clinical efficacy of immunotherapy. The higher TIDE prediction score is attributed to the severe immune escape, which reveals that the patients are unlikely to benefit from ICI treatment. MSI and rejection differed from high-risk to low-risk subgroups (Fig. 7C–D), however, TIDE and dysfunction had no obvious distinction between low-risk and high-risk subgroups (Fig. 7E-F).

**Discussion**

Immune infiltrates in the glioma microenvironment participate in its occurrence and development. Meanwhile, protein markers have been found that can predict the prognosis of patients has attracted particular attention. Therefore, it is of significance to explore the association between protein markers and immune infiltration, as well as their prognostic value for glioma patients undergoing immunotherapy.

In this research, 42 proteins were screened out by cross-overlap analysis of proteins in tumor tissues of TCGA database and Renji cohort, then, six proteins signature was established by the LASSO mathematical model, which contains VAV1, IGFBP2, COG3, MSH2, BAX, and SOX. The 6-protein signature had a better prognosis value in the OS of glioma and was associated with immune cells and function in the environment of glioma. In conclusion, the model is helpful for individualized therapy and management of tumors with glioma after the operation.

The signature of the six proteins consists of VAV1, IGFBP2, COG3, MSH2, BAX, and SOX, each of which plays a crucial role in tumor immunity or glioma prognosis. VAV, GDP/GTP exchange factors for Rho/Rac proteins, was one of the best known Rho/Rac activator families and promote carcinogenesis by participating in the regulation of cell migration and cytoskeletal dynamics (23, 24). In a study of 59 patients, VAV1 transcripts were observed by immunohistochemistry in 46% of high-grade gliomas (HGG) in GBM, which demonstrates the expression of the VAV1 protooncogene in the microenvironment of High-grade gliomas (HGGs) (25). IGFBP2, an independent poor prognostic biomarker in GBM patients, high expression of which predicts unfavorable survival in GBM patients. Immunosuppression is the main feature of GBMs with high IGFBP2, which is strongly synergistic with classic immunosuppressive biomarkers, including ANXA1, CHI3L1, LGALS1, LGALS3, TIMP1, TNFRSF1A, and VEGFA. The mechanism is that IGFBP2 could affect the immune response of tumor tissues by regulating NF-κB and IGF signaling pathways (26). Compared to the healthy brain tissue, CADPS E/G and COG3 I/V (with > 15% editing increase in cancer) validated by Sanger sequencing are highly edited in GBM; It has also been shown that COG3 I/V over-expression may be a pre-neoplastic event that promotes proliferation and migration of glioblastoma cells, with higher editing levels at this site (≥ 40%) related to poor prognosis (27). COG3 I/V editing might become a new clinical prognostic factor in GBM patients. MSH2 is prevalent in most cancers and directs the production of proteins that modulates DNA repair, thus the MSH2 gene was also considered an oncogene (28). Mir-1298-5p plays a significant role in glioma cells via targeting MSH2, which could promote the immunosuppressive effect of myeloid-derived suppressor cells (MDSCs), also the occurrence of glioma (29). Bax is one of the short-lived proteins in tumors that plays a crucial role in therapy-associated apoptosis and the sensitivity of glioma cells to spontaneous responses, also, is one of the potential molecular targets for the diagnosis and treatment of glioma. The trichothiodystrophy group A protein (TTDA) inhibits p53-Bax /BCL2 mitochondrial apoptosis pathway in glioma cells by
interacting with the p53 gene and regulating its transcription (30). However, some studies show that reduced expression of Bax is associated with poor clinical prognosis in gliomas patients and SMBA1 (small molecule Bax agonist 1), which is a small molecule activator of Bax, has anti-proliferative effects on GBM cells by activating the intrinsic apoptotic pathway (31, 32). The SOX transcription factors are involved in regulating diverse cellular processes, which exists a complex regulatory network interacting with microRNA (33). Almost always SOX genes are expressed in GBM, and SOX transcription factors (TFs) are related to patient prognosis. Innovative therapies targeting SOX TFs could become a tool to fight GBM because of their role in maintaining glioma stem cells (GSCs) and differentiation (34). In summary, the 6 oncoproteins played important roles in the immune environment of glioma.

There exists an innate immune system in the central nervous system (CNS), meanwhile, the brain does have immunological surveillance, and innate immunity-related molecules express in the brain and influence the immune microenvironment (35). Immune responses in the brain progress more slowly than in peripheral tissues (36). In neuroinflammation or injury, cells continuously release cytokines and chemokines that impair the BBB. Through these cytokines, peripheral immune cells are recruited to penetrate the damaged blood-brain barrier and reach the site of injury (37). Infiltration by immune cells is a hallmark of virtually every tumor (38). Tumor infiltrating immune cells play an important role in tumor suppression or tumor proliferation in the tumor microenvironment (39). Cancer immune editing consists of elimination, balance, and escape. One of the escape stages promotes the tumor cells' progress to a clinical stage of cancer and contributed to tumor-induced immune suppression or immune degeneration (40, 41). Glioma seeks to escape immunological surveillance through a deadly symbiotic collaboration.

Microglia cells were the main immune cells in the brain (42, 43), and have also been confirmed as an immune infiltrating cell in CNS tumors' microenvironment (39). Tumor cells secrete CSF-1 to promote the aggregation of microglia, and in turn, microglia release epidermal growth factor (EGF) and stress-inducible protein 1 (STI1) to promote glioma proliferation, invasion, and metastasis (20, 44, 45). TAMs can release cytokines and growth factors according to cancer cell activity in the tumor microenvironment, which promotes glioma growth and invasion (46). NK could use soluble molecules of the tumor necrosis factor (TNF) family to kill tumor cells (47). Mature dendritic cells (mDC) could induce tumor-specific T cell activation by releasing cytokines and chemokines (48). Treg cells that express CD25 and FoxP3 suppress the proliferation of other T cells, which promote tumor invasion (49, 50). Foxp3 and VISTA are highly expressed in advanced human gliomas and shorten the patient's survival time. However, preferential recruitment of Treg is associated with a subsequently poor prognosis (51). Different types of infiltrating immune cell populations play a role in inhibiting or promoting malignancy depending on the type of cancer, or even the same tumor type in different patients or different stages in the same patient (diagnosis and recurrence) (52, 53). The brain is under constant immune surveillance and communicates with the surrounding immune system, making immunotherapy possible. As a revolution in cancer treatment, immunotherapy could penetrate the blood-brain barrier. The upregulation of multiple immune checkpoints and an increased fraction of Tregs are highly features of the brain tumor microenvironment (TME), which warrants the investigation of immune checkpoint inhibitors (ICIs) as a potential means to restore T-cell responses (54–57). The efficacy of ICI in patients with glioblastoma is limited, especially the
The efficacy of the PD-1/PD-L1 antibody in the therapy of GBM remains elusive (58, 59). The combination of CTLA-4 and PD-1 was shown to cure 75% of immunocompetent mouse GBM models, including advanced tumors (60). In a preclinical research, the combination of PD-1 blockade and localized radiation could triple the median survival rate of glioma mice, even result in long-term survival, compared with a single treatment (61). We found that PD1 expression differed among different risk score groups, and the possibility of immune escape could be achieved from the score to predict the benefit of ICI treatment.

There were also some limitations in the research. Firstly, there were no non-tumor samples in the TCGA database of glioma, therefore, differentially expressed proteins were not obtained except in the Renji cohort. Next, tumor infiltrating immune cells were not assessed in fresh glioma specimens of patients, and more fresh specimens ought to be obtained to elucidate the effect of this 6-protein signature on predicting immune cell infiltration. All in all, the mechanism of these six proteins in tumorigenesis and development should also be explored in future studies.

**Conclusion**

Six proteins signature was constructed from TCGA and Renji cohort. The results of our analysis have the following clinical implications: First of all, it could be applied to predict the prognosis of individual glioma therapy. Secondly, the immune cell infiltration degree and immune function activity degree of all kinds of immune cells could be evaluated through the risk model. Last but not the least, this model could be used to distinguish the degree of benefit from immunotherapy.

**Abbreviations**

GEO
Gene Expression Omnibus
TCGA
The Cancer Genome Atlas
LASSO
The least absolute shrinkage and selection operator
OS
overall survival
TIDE
tumor immune dysfunction and exclusion
TIS
tumor inflammation signature
DEGs
differentially expressed genes
ROC
the receiver operating characteristic
MSI
Declarations

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Review Committee of Renji Hospital, School of Medicine, Shanghai Jiaotong University. The patients/participants provided their written informed consent to participate in this study.

Conflict of Interests

The authors declare that this study was conducted in the absence of any commercial or financial relationship that could be interpreted as a potential conflict of interest.

Author contributions

XYS had the idea and drafted the manuscript. HYT and HG collected the data and prepared the figures and graphs. JZ and DXZ provided clinical information about patients and statistical suggestions. JL provided clinical specimens. YHB and HG supervised the research and revised the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability statement

The datasets presented in this study can be found in online repositories: https://www.scidb.cn/s/FrqqAj

References


**Figures**
Identification of differentially expressed protein and functional analysis in glioma samples from Renji cohort. (A) Biological processes (BP), Molecular Function (MF) and Cellular Component (CC) of glioma samples from Renji cohort. (B) KEGG pathway analysis of glioma samples from Renji cohort. (C) Heatmap of glioma samples. (D) Volcano plots of differentially expressed proteins (DEPs) in Renji cohort (X-axis: log2(FC); Y-axis: -log10(FDR) for each protein. Proteins with FDR 0.05 and FC >1.0 or <-1.0 were
considered as DEPs in each series. Green: down-regulated proteins; Grey: non-differential Proteins; Red: up-regulated proteins). (E) KEGG pathway classification in UP or Down proteins of glioma samples from Renji cohort, respectively.

**Figure 2**

A

![Graph A](image1)

B

![Graph B](image2)
Construction of a 6-protein signature from the TCGA cohort. (A) Lambda of the risk score model. (B) LASSO model at optimal lambda value.

Figure 3

Verification of the prognostic risk score model based on a 6-protein signature in glioma. (A) K–M survival curves of the TCGA Train set. (B) K–M survival curves of the TCGA Test set. (C) Risk score curves of the TCGA Train set. (D) Risk score curves of the TCGA Test set. (E) Dot diagrams of the TCGA Train set. (F) Dot diagrams of the TCGA Test set.
Figure 4

Differential analysis of immune cells between high and low risk groups. (A) B cells naïve, (B) Macrophages M0, (C) Macrophages M1, (D) Macrophages M2, (E) T cells CD8, (F) T cells follicular helper, (G) T cells gamma delta, (H) T cells regulatory (Tregs), (I) NK cells activated.
The Kaplan–Meier analysis of different immune cells in the risk model. (A) The KM curve of B cells naïve, (B) The KM curve of Neutrophils, (C) The KM curve of Macrophages M0, (D) The KM curve of Macrophages M1, (E) The KM curve of Macrophages M2, (F) The KM curve of NK cells resting, (G) The KM curve of T cells follicular helper, (H) The KM curve of T cells regulatory (Tregs), (I) The KM curve of NK cells activated, (J) The KM curve of Mast cells activated, (K) The KM curve of Monocytes, (L) The KM curve of Eosinophils.
Figure 6

The Kaplan–Meier survival analysis for immune functions. (A) The KM curve of CD8+ T cells. (B) The KM curve of B cells. (C) The KM curve of T cell co-inhibition. (D) The KM curve of T cell co-stimulation. (E) The KM curve of T helper cells. (F) The KM curve of Tfh cells. (G) The KM curve of Th1 cells. (H) The KM curve of Th2 cells. (I) The KM curve of TIL. (J) The KM curve of Treg. (K) The KM curve of Type I IFN response. (L) The KM curve of Type II IFN response. (*p < 0.05, ** p < 0.01)
Figure 7

The prognostic value of 6-proteins signature in patients with anti-PD-L1 therapy. (A) PD-L1 in different risk score subgroups, (B) Correlations between the prognostic signature-derived risk score and PD-L1, (C) MSI in different risk score subgroups, (D) Exclusion score in different risk score subgroups, (E) TIDE in different risk score subgroups, (F) T cell dysfunction in different risk score subgroups.
Supplementary Files

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