Identify an Innovative Fatty Acid Metabolism-Related Gene in Head and Neck Squamous Cell Carcinoma

Kai Fu
The Fourth Hospital of Hebei Medical University and Hebei Tumor Hospital

Lin Li
Hebei General Hospital

Tengfei Liu
Xingtai People's Hospital

Shaoning Yin (✉ hebmuysn@163.com)
The Fourth Hospital of Hebei Medical University and Hebei Tumor Hospital

Research Article

Keywords: PTGDS, head and neck squamous cell carcinoma, fatty acid metabolism-related genes, prognostic signature, tumor microenvironment, immunotherapy

Posted Date: March 17th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2684142/v1

License: ☕️ ☀️ This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

**Background:** Head and neck squamous cell carcinomas (HNSCCs) are the sixth largest group of malignancies worldwide. Due to the highly aggressive, heterogeneousness and tumor microenvironment, the variable prognosis of HNSCC patients is changeable. Fatty acid metabolism-related genes (FAMGs) play a vital role in the development of malignant tumors, but the role in HNSCC is still unclear. The purpose of this study was to establish a reliable prognostic model based on FAMGs for evaluating the prognosis and immunotherapy of HNSCC patients and find the key prognostic genes to provide guidance for the early diagnosis and treatment.

**Methods:** We obtained cancer-related data from various public databases. The FAMGs risk score model was established and proved by a combination of univariate Cox analysis and least absolute shrinkage and selection operator (LASSO) regression analysis. Combining risk scores and clinical characteristics, a nomogram was created and validated. Subsequently, the function, immune difference, immune infiltration, enrichment analysis, and hub genes of the groups with high- and low-risk scores were analyzed. Consequently, the mode's validity was evaluated comprehensively by combining single gene analysis and pan-cancer analysis.

**Results:** we screened out 73 differentially expressed FAGMs and 9 genes associated with prognosis to construct a prognostic risk score model for genes related to fatty acid metabolism. The FAMGs signature was an independent prognostic factor for HNSCC, and patients in the low-risk group had higher overall survival (OS) than those in the high-risk group. In addition, we found differences in immune cell infiltration and enrich pathways between the different risk score groups. Finally, through the risk assessment model, combined with multiple databases, PTGDS, a high-risk and prognosis-related gene, was screened. And it showed a trend of low expression in many cancers, which predicted the prognosis of many cancers, especially in HNSCC.

**Conclusion:** Metabolism-related genes affect the prognosis and survival of patients with HNSCC through affecting tumor microenvironment. And PTGDS can predict the survival and prognosis of cancer patients as an independent effective prognostic factor, particularly in HNSCC.

Introduction

Head and neck squamous cell carcinomas (HNSCCs) are the sixth most common malignant tumor in the world\(^1,2\), which originated from the mucosal epithelium in the oral cavity, pharynx and larynx\(^3,4\). Despite remarkable progress has been made recently in both basic and clinical research, HNSCC remains one of the leading causes of mortality with a 5-year survival rate of 50\(^%\)\(^5\). Due to high rates of lymph node metastasis and recurrence of HNSCC, most patients have an unfavorable prognosis, especially for the advanced cases. Therefore, a clearer understanding of novel molecular markers of HNSCC is urgently needed to help us find more effective targets for HNSCC diagnosis and therapy.
Fatty acid metabolism, essential for various biological activities, such as cell membrane formation, energy storage, and signaling molecule generation in oncogenesis, has earned huge attention\textsuperscript{6, 7}. Fatty acid metabolism-related genes (FAMGs) are important guarantee for the continuous growth, proliferation and migration of cancer cells\textsuperscript{8, 9}. At present, metabolic reprogramming is considered to play a pivotal role in anticancer therapeutic resistance and a key feature of tumorigenesis\textsuperscript{10, 11}, which occurs correlates with cellular stress and immune response in HNSCC\textsuperscript{12}. Studies have shown that microRNAs involved with fatty acid metabolism are strongly linked to the prognosis of HNSCC patients\textsuperscript{13}. Fatty acid oxidation (FAO)-related enzymes and long-chain acyl-CoA dehydrogenase (LCAD) have a protective effect on overall survival in advanced HNSCC patients\textsuperscript{14}. In addition, fatty acid metabolism-related gene expression-based risk signature could predict the prognosis of HNSCC independently, and has a certain therapeutic guidance value\textsuperscript{15}.

To our knowledge, although there are a large number of studies exploring the mechanism and role of fatty acid metabolism in various cancers, research on determining the prognosis of HNSCC as a target for immunotherapy through FAMGs is still not clear. In this study, we introduced FAMGs associated with the prognosis of HNSC, and also carry out several follow-up analyses to explore the underlying mechanisms. In short, we aim to find accurate biomarkers and therapeutic targets of HNSCC to facilitate personalized treatment.

**Materials And Methods**

**Data Collection**

The mRNA-sequencing and clinical data of HNSC were collected from TCGA database (https://cancergenome.nih.gov/). The microarray data profiles of GSE41613 were obtained from GEO database (https://www.ncbi.nlm.nih.gov/geo/) as a validation set. 309 fatty acid metabolism related-genes were sourced from previous literature\textsuperscript{16} (Supplementary Table 1). The cell line mRNA expression matrix of tumors was obtained from the CCLE dataset (https://portals.broadinstitute.org/ccle). Tumor Immune Dysfunction and Exclusion (TIDE) website (http://tide.dfci.harvard.edu/) was used to predict response to cancer immunotherapy (anti-PD1 and anti-CTLA4). The expression of PTGDS in HNSC was verified by TIMER (https://cistrome.shinyapps.io/timer/) website.

**Development and Validation of a Prognostic FAMGs Signature**

The “Limma” R package was exploited to examine the expression of FAMGs between normal and tumor samples. Univariate Cox regression analysis was used to construct the risk model to screen for prognostically associated FAMGs in the HNSCC cohort. Subsequently, FAMGs ($P < 0.05$) significantly associated with prognosis with HNSCC were enrolled the Least Absolute Shrinkage and Selection Operator (LASSO) COX regression models, and the key genes and regression coefficients were determined by the “glmnet” R package. Mutations and associations of genes were analyzed by the “maftools” R package.
The risk fraction was generated by the formula: risk fraction = risk score = esum (each gene’s expression \( \times \) corresponding coefficient)\(^{17}\). The “Maftools” R package was used to analysis the mutations and associations of genes in the HNSC samples.

All samples were divided into low-risk and high-risk groups according to the median risk score of samples from TCGA. Moreover, we used the “limma” R package to perform principal component analysis (PCA) on mRNA expression, and the “survivalROC” R package to assess the predictive power of genes by time-dependent ROC curve analysis. Moreover, Kaplan–Meier analysis was used to compare the differences in OS between low- and high-risk groups.

**The Relationship of Clinical Characteristics and Risk Scores**

The nomogram for predicting OS was built by the “rms” R package based on the gene expression and clinical data of HNSC patients. The validity of the nomogram was predicted using time-dependent calibration curves and AUC curves. Univariate and multivariate Cox regression analyzes were performed to evaluate whether the prognostic risk score model could independently serve as a predictor of OS in HNSC patients. The “limma” R package was adopted to determine the relationship between risk scores and clinical characteristics.

**Immune Landscape and Functional Enrichment Analyses**

The “GSVA” R package was used to quantify immune cell infiltration and immune-related functions. And the “clusterProfiler” R package utilized to subjected Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis.

**PPI Network**

We analyzed prognostic fatty acid metabolism-related DEGs by the STRING website (https://cn.string-db.org/) to build the PPI network, and Cytoscape software to obtain the hub genes.

**Results**

**Identification of Fatty Acid Pathway Risk Signature in HNSC**

To explore the FAMGs in HNSC, 73 FAMGs were selected from TCGA-HNSC patients (Fig. 1A). Compared with normal samples, 27 upregulated genes and 46 downregulated genes (Fig. 1B, FDR < 0.05 and |logFC| > 1). Next, a total of 9 genes with prognostic value were screened (\( P < 0.05 \), Fig. 1C). Gene signatures combined with somatic mutation profiles were able to increase prognostic power\(^{18}\), so we went on to explore the somatic mutation profile of 9 genes associated with prognosis. Among HNSC samples, 33 showed mutations in FAMGs, with a frequency of 6.47%, ACACB had the highest mutation frequency (Fig. 1D). Further analysis showed mutational co-occurrence relationship between ACACB and ACADL (Fig. 1E).
Besides these, the identified 9 genes with prognostic value (PTGDS, PHYH, ACSBG2, ACSM3, SMS, ACADL, ACACB, LGALS1, and INMT, Table 1) were used to construct the prognostic risk score model (Fig. 2A and 2B). The formula for risk-score calculation was established as follows: risk score = PTGDS × (-0.281726688635234) + PHYH × (0.214264437990027) + ACSBG2 × (-2.34123344624269) + ACSM3 × (0.279576196804868) + SMS × (0.177081518154732) + ACADL × (0.534288570425711) + ACACB × (-0.171772020486959) + LGALS1 × (0.0501242441953272) + INMT × (-0.124529055232544). We performed PCA to evaluate sample heterogeneity, and the results indicated a significant difference (Fig. 2C and 2D). According to the cut-off value of the risk score in training set, patients were ranked and divided into high-risk score groups and low-risk score groups, we observed HNSC patients in the high-risk group had worse OS than that of patients with low-risk score ($P < 0.001$, Fig. 2E), which was also validated by GSE41613 datasets ($P = 0.001$, Fig. 2F). Furthermore, while comparing the difference in progression-free survival (PFS) between the two risk groups, the low-risk groups had significantly superior PFS ($P < 0.001$, Fig. 2G).

We then went on to explore the stability and reliability of the risk score as a clinical indicator. 1-year (AUC = 0.673), 2-year (AUC = 0.667), 3-year (AUC = 0.634) survival assessments were performed for AUC (Fig. 3A). In addition, the forest plot showed similar results to the Fig. 3B., age ($P < 0.001$, AUC 0.563), pathological stage ($P < 0.001$, AUC = 0.594), and risk score ($P < 0.001$, AUC = 0.634) clearly correlated with OS (Fig. 3C and Fig. 3D).

**Clinical Features of the Risk Signature**

We first verified that the distribution of risk scores in immune subtype, tumor grades, pathological stage, M staging, T staging and N staging of samples in TCGA cohort. Although there were no statistically significant correlations between risk scores and tumor grades, M staging, and N staging (Fig. 4B, 4C and 4F), risk scores were correlated with T staging and immune subtype to some extent (Fig. 4A and 4D). Patients of T3 had higher risk scores than those of T1/T2 ($P < 0.05$). Patients of N0 had higher risk scores than those of lower N2 staging ($P < 0.05$). Regarding the pathological stage, risk scores also increased in stage III/IV patients compared with stage I patients ($P < 0.05$, Fig. 4E). The lack of control group limits the ability to draw definitive conclusions.

Moreover, we combined the clinical characteristics to build nomograms (age, gender, pathological stages, TMN staging, tumor grades, and risk scores, Fig. 4G), and used the AUC to evaluate the predictive power of the nomogram. The results showed that nomogram model (AUC = 0.793, Supplemental Fig. 1) was constructed to make more accurately personalized predictions for HNSC patients. Finally, both the univariate and multivariate Cox regression analysis indicated that the stage and nomogram were independent prognostic factors. (Fig. 4H and 4I).

**Immune Landscape and Functional Enrichment Analyses of the Risk Signature**

Given the immunotherapy has altered treatment strategy of HNSC, we explored the relationship between immune factors and the risk score model. Firstly, we validated the relationship between risk score and tumor-infiltrating immune cells based on the CIBERSORT algorithm. The boxplot revealed that the low-risk
group had more immune cell infiltration. However, resting CD4 + memory T cells (P < 0.05), M0 macrophages (P < 0.01), M2 macrophages (P < 0.01), activated mast cells (P < 0.001) and resting NK cells (P < 0.05) were higher enriched in the high-risk group (Fig. 5A). In addition, the low-risk group had more active immune-related functions, including APC co-stimulation (P < 0.001), CCR (P < 0.01), checkpoint (P < 0.001), cytolytic activity (P < 0.001), HLA (P < 0.01), inflammation promotion (P < 0.001), MHC-class-I (P < 0.01), T cell co-inhibition (P < 0.001), T cell co-stimulation (P < 0.001) and Type-II-IFN-Response (P < 0.001) (Fig. 5B). Collectively, these results meant that low-risk patients may respond better to immunotherapy.

To interpret differential biological functions between the high- and low-risk score groups, we conducted GSVA enrichment analysis, which showed the model genes were significantly enriched in most signaling oncogenic pathways (Fig. 6A). Next, GO and KEGG analyses were performed for further functional analysis between the high- and low-risk score groups. The genes were engaged in immunoglobulin complex, antigen binding, immunoglobulin receptor binding, etc. according to GO findings (Fig. 6B). These genes were enriched to be abundant in cytokine-cytokine receptor interaction cell adhesion molecules, etc. according to KEGG findings (Fig. 6C).

In the previous content, we used a variety of assays to validate the value of the risk model composed of 9 fatty acid metabolism genes. To interpret the expression patterns of DEGs in the low- and high-risk groups, we used the online STRING database and Cytoscape program. CytoHubba was used to analyze the entire PPI network and select top 10 hub genes, which were ranked according to the degree method as CD79B, MYL1, CD79A, CD5, SELL, CSRP3, MYL2 and VCAM1 (Fig. 6D).

**PTGDS Is an Independent Prognostic Gene for HNSC Patients**

After a series of preliminary studies, following hypothesis was proposed: PTGDS is a potential biomarker in patients with HNSC. Compared with the normal group, the PTGDS in tumor tissue was significantly under-expressed, (P < 0.001, Fig. 7A and 7B). According to multi-clinical classifications, PTGDS levels were associated with G staging and T staging (Fig. 7C and 7E), but not with pathological stage or N staging (Fig. 7D and 7F). Due to the accuracy of T staging is considerably high, moreover, the heat map of risk scores also showed good results (Fig. 7G). The KM survival curves showed that the high expression group had better OS compared with the low expression group (Fig. 7I). 1-year AUS = 0.631, 3-year AUC = 0.579 and 5-year AUC = 0.556 (Fig. 7J). The above findings showed that low expression of PTGDS was associated with poor prognoses in patients with HNSC.

We used TIMER to evaluate the correlation between PTGDS expression and TIL, including CD4 + T cells, B cells, macrophages, dendritic cells and neutrophils. The results showed that the PTGDS was negatively correlated with tumor purity, but with B cells, CD8 + T cells, and CD4 + T cells, neutrophils and dendritic cells were positively correlated (Fig. 8A). In order to further explore the role of PTGDS in immunomodulation, we also exploited immunotherapy analysis between the low- and high-risk score groups and found that combination of the anti-CTLA4 and anti-PD-1 therapy had more potent efficacy (P = 0.0067, Fig. 8B).
Pan-Cancer Integrated Analysis Identification of PTGDS

PTGDS, as a potent endogenous nociceptive modulator, is quite contradictory in tumorigenesis and cancer progression, we were interested in whether changes of PTGDS expression predict the prognosis of other cancers. PTGDS was selected for subsequent studies to confirm the functions of the prognostic genes. Firstly, we evaluated PTGDS gene expression in the 33 pairs of cancer and normal tissue samples. Results showed that PTGDS was the direction of decreasing trend in multiple human cancers (Fig. 9A), including bladder urothelial carcinoma (BLCA), breast invasive carcinoma (BRCA), colon adenocarcinoma (COAD), head and neck squamous cell carcinoma (HNSC), kidney chromophobe (KICH), kidney renal clear cell carcinoma (KIRC), kidney renal papillary cell carcinoma (KIRP), lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), prostate adenocarcinoma (PRAD), rectum adenocarcinoma (READ), stomach adenocarcinoma (STAD), thyroid carcinoma (THCA), and uterine corpus endometrial carcinoma (UCEC) \((P < 0.05)\). Such data indicated that PTGDS may play a critical role in cancer diagnostics. Analogous results were obtained in CCLE dataset (Fig. 9B).

The prognosis of cancer patients is closely related to the response to treatment. To further elucidate the relationship between PTGDS expression and the prognosis, we conducted a pan-cancer survival analysis with OS of 10228 patients. we found that PTGDS was related to lower OS in BRCA, ESCA, COAD, KIPC, DLBC, SARC, UCEC, and HNSC \((P < 0.05\), Fig. 9C). Similarly, PFS analysis (Fig. 9D) also showed a negative correlation between high PTGDS expression and prognosis for UCEC, SARC, BRCA, and HNSC \((P < 0.05)\).

Tumor-infiltrating immune cells are closely associated with the occurrence and development of tumors. the CIBERSORT, TIMER, EPIQ, QUANTISEQ, and MCPandscape algorithms were applied (Supplemental Fig. 1). We observed a significant statistical correlation between PTGDS and tumor immune cell infiltration. The results implied that PTGDS expression was markedly correlated with the infiltrating level of B cells in 18 types of cancer, CD4 T cells in 25 types of cancer, CD8 T cells in 14 types of cancer, macrophages in 17 types of cancer, neutrophils in 17 types of cancer, and DCs in 19 types of cancer (Fig. 10A). The other algorithms revealed similar results (Fig. 10B). In addition, we also found that PTGDS was significantly associated with multiple immune checkpoint genes (Fig. 10C).

TMB and MSI have gradually emerged as biomarkers related to the immunotherapy response. Cancer immunity can vary depending on genetic mutations. Thus, we further analyzed correlations between PTGDS and TMB/MSI. We observed a negative correlation between PTGDS expression and TMB for PRAD, STAD, LGG, THCA, LUAD, THYM, SKCM, SARC, LIHC, HNSC, LUSC, GBM, PAAD, and LGG \((P < 0.05\), Fig. 10D). PTGDS expression was also negative correlated with MSI in STAD, TGCT, READ, VCEU, and LIHC, but we found a positive correlation depicted between PTGDS and HNSC \((P < 0.05\), Fig. 10E). This observation deserves closer investigations, especially in relevance for HNSC patients.

Discussion
HNSCC is a heterogeneous group of cancers that caused by squamous cell abnormalities\(^{19}\). The long-time survival rate of HNSCC remains poor due to the high rate of recurrence and distant metastasis\(^{20}\). It has been suggested that metabolic reprogramming is a cancer hallmark, and abnormal fatty acid metabolism is related to the malignant phenotype in HNSCC, including chemoresistance, relapse and metastasis\(^ {21}\). Therefore, we build a risk score model to predict HNSCC patients' survival time by analyzing the differential expression of FAMGs, and find possible therapeutic targets and prognostic markers of fatty acid metabolism for HNSCC patients.

In this study, 73 differentially expressed fatty acid metabolism genes were selected, of which 46 genes were down-regulated and 27 genes were up-regulated. Then identified 9 key genes which were associated with prognosis, including PTGDS, PHYH, ACSBG2, ACSM3, SMS, ACADL, ACACB, LGALS1, and INMT, that may become useful prognostic biomarkers in the clinical management of HNSCC patients. We found patients in the high-risk group had worse OS than those in the low-risk group. Importantly, FAMGs-based risk signature showed great accuracy and independence according to univariate and multivariate Cox regression analyses.

Recently, studies have suggested that HNSCC is rich with infiltrated immune cells, the progression and prognosis of cancer are tightly related to immune cell infiltration\(^ {22}\). Furthermore, fatty acid metabolism is directed at supporting specific cell functions, since the final outcome of an immune response is determined by cell metabolism\(^ {23}\). Therefore, the relationship between the risk score and the infiltration of immune cells is highly warranted. Our results showed that several immune cells, including T Cell, B Cell, and macrophage cells were associated with the risk score significantly. In addition, GO and KEGG, enrichment analyses were performed to further explore potential molecular mechanism of the model, signal pathways (immunoglobulin complex, cytokine-cytokine receptor interaction cell adhesion molecules and so on) involving the tumorigenesis were enriched in the high-risk group. GSVA enrichment showed the model genes were significantly enriched in most signaling oncogenic pathways, suggesting these risk genes play a key role in HNSCC. All these findings provide ideas for our future mechanism research.

Glycoprotein prostaglandin D2 synthase (PTGDS), as a novel prognostic gene in HNSCC, is a member of the lipocalin superfamily and located in human chromosome 9 (9q34.2 ~ 34.3)\(^ {24, 25}\). It also is a bifunctional protein that catalyzes PGD2 production and transports lipophilic substances and plays dual roles in prostaglandins metabolism and lipid transport. It was previously reported that PTGDS expression is overexpressed and the level directly correlates with tumor size, metastasis and poor prognosis in some solid and hematological tumors\(^ {26, 27}\). Whereas, in our study the PTGDS expression was lower in cancer tissues, including malignant melanomas, hepatocellular adenoma, and gastric carcinomas. Other experiments have also shown PTGDS is lower expression in cancer, which has the anti-proliferation and anti-invasion effects\(^ {28, 29}\). We think that such contradictory results may be related to missing data or insufficient sample quantity. Moreover, recent investigations showed that PTGDS acts as modulators of PPAR\(\gamma\), MAPK, and STAT3 pathways, which are associated with the pathogenesis of hematological
malignancy\textsuperscript{30, 31}. Therefore, PTGDS is associated with unfavorable therapeutic efficiency and poor prognosis.

Based on our results we find the novel fatty acid metabolism prognostic signature of PTGDS, which can predict the survival and prognosis of cancer patients as an independent effective prognostic factor, particularly in HNSCC. Meanwhile, our data may explain how fatty acid metabolism-related genes affect the prognosis and survival of patients with HNSCC through affecting tumor microenvironment.

References


**Table**

Table 1 is not available with this version.

**Supplementary Information**

Supplemental Table 1 and figure 1 are not available with this version.

**Figures**
Identification of candidate FAMGs. (A) Heat map of the difference in mRNA expression between tumor samples and normal samples. Red for high expression, blue for low expression. (B) Volcano map of FAMGs with differential expression. Red dots indicate upregulated genes, black dots indicate insignificant differences, and green dots indicate downregulated genes. (C) The forest plot shows the results of the
univariate Cox regression analysis. (D) The mutation frequency of candidate genes in 506 HNSC samples from the TCGA cohort. (E) Co-occurrence and exclusion of mutation analyses for candidate genes.

Figure 2
Prognostic risk score model established in the TCGA cohort. (A) LASSO coefficients of the 9 fatty acid metabolism-related genes. (B) Identification of genes for development of prognostic risk score model. (C)
Principal component analysis of genes involved in FAMGs. (D) Principal component analysis of genes involved in model genes. (E) Overall survival of high- and low-risk groups in the TCGA cohorts. (F) Overall survival of high-and low-risk groups in the GEO cohorts. (G) Comparison of progression-free survival between patients in the high- and low-risk groups in the TCGA cohorts.

Figure 3

(A) Time-dependent ROC curves at separately one year, three years, and five years. (B) ROC curves for risk score and clinical features. (C, D) The forest plots show the results of univariate (C) and multivariate (D) Cox regression analysis in the TCGA cohort.
Figure 4

Development of a nomogram for OS prediction. (A) The relationship between risk score and immune subtype. (B) The relationship between risk score and grade. (C) The relationship between risk score and M staging. (D) The relationship between risk score and T staging. (E) The relationship between risk score and pathological staging. (F) The relationship between risk score and N staging. (G) The nomogram for
predicting survival in HNSC. (H, I) The forest plots show the results of univariate (H) and multivariate (I) Cox regression analysis.

Figure 5

Differences in immunization between the high-risk and low-risk groups. (A) Immune cell infiltration in the high-risk and low-risk groups. (B) Comparison of immune function between the high-risk and low-risk
Figure 6

Functional analysis of DEGs and PPI network. (A) Heatmap is showing the GSVA of DEGs. (B) Bar plot for GO analysis of DEGs. (C) Bar plot for KEGG analysis of DEGs. (D) PPI network of risk differential genes.
Figure 7

Prognostic analysis of PTGDS in the TCGA cohort. (A) PTGDS expression in controls and HNSC patients. (B) Pairwise analysis of PTGDS expression in controls and HNSC patients. (C-F) Results of the clinical correlation analysis. Differences in risk scores by T staging, N staging stage, and grade. (G) The heatmap of clinical correlation analysis. (H) Correlation of PTGDS expression with patient survival. (I) KM survival curve of PTGDS. (J) ROC survival curve of PTGDS.
Figure 8

Figure 9

The expression level of PTGDS in human cancer. (A) Pan-cancer analysis in TCGA cohort (B) Pan-cancer analysis in CCLE cohort (C, D) Prognosis of PTGDS in Pan-cancer analysis.
Figure 10

Relationship between PTGDS and immunity in pan-cancer analysis. (A) Correlation of PTGDS expression with immune infiltrates based on the TIMER analysis in Pan-cancer analysis. (B) Correlation of PTGDS expression with immune infiltrates based on the CIBERSORT analysis in Pan-cancer analysis. (C) Pan-cancer analysis of immune checkpoint genes and PTGDS expression. (D) Pan-cancer analysis of TMB and PTGDS expression. (D) Pan-cancer analysis of MIS and PTGDS expression.