Title: Age-specific prognostic hub genes associated with immune cell infiltration in glioblastoma multiforme: An analysis of TCGA data

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Abstract:

Introduction

Glioblastoma multiforme (GBM) is the most common malignant brain tumor and carries a poor prognosis with median survival time (MST) of approximately 18-20 months. Increasing evidence has revealed that infiltrating immune cells and other stromal components in the tumor microenvironment (TME) are associated with prognosis of GBM. The present study was conducted to identify age group-specific prognostic hub genes associated immune cell infiltration in GBM patients.

Methods

We extracted clinical and gene expression data [based on RNA-Sequencing (RNA-Seq) and microarray] of 593 primary GBM patients from The Cancer Genome Atlas (TCGA) (www.cancergenome.nih.gov). For analysis, the data was distributed into four age groups (10-44 years, 45-54 years, 55-64 years, and > 65 years of age). Age-specific gene expression profiles were analyzed using differentially expressed genes (DEGs); protein-protein interaction (PPI) network was constructed to identify top hub genes from DEGs. Prognostic hub genes were identified employing Kaplan-Meier survival analysis. The enrichment level of various immune signatures were identified using the single-sample gene-set enrichment analysis (ssGSEA) score. Spearman's correlations were identified between the ssGSEA score and the expression levels of selected hub genes.

Results

Kaplan-Meier analysis revealed a significantly decreased survival with advancing age (log rank test, $p < 0.0001$). Based on RNA-Seq analysis, ADORA1, CFTR, F3, FBP1, GPR37, GPRC5A, KIF16B, MT1H, OXTR, and SFN hub genes was consistently associated with poor survival in GBM patients' age group > 65 years. Most of the prognostic genes were correlated with CD4+ T-cells, macrophages, T-cell exhaustion, TILLs, TREGs and some hub genes were negatively correlated with immune stimulatory CD8+ T-cells and B-cells.

Conclusion

The transcriptomic analysis of TCGA data identified prognostic hub genes associated with immune cell infiltration in tumor microenvironment in GBM patients.

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Non-expert summary: This was an original research study which identified genes associated with shorter survival time in older GBM patients. We further report on immunological mechanisms responsible for this finding.