SAA1

Serum amyloid A1 (SAA1) is a sensitive acute phase reactant primarily produced by the liver in response to acute inflammation. We have recently shown that SAA affects proliferation, migration, and invasion of glioblastoma cell lines, which suggest its participation in the malignant process. Consistently, levels of SAA have been used as a non-invasive biomarker for the prognosis of many cancers. In this study, we aimed to investigate SAA serum levels and expression of SAA genes in human astrocytomas tissues. Serum and tissue samples were obtained from patients with astrocytoma grades I to III and glioblastoma (Glioblastoma or grade IV). Levels of circulating SAA were significantly higher in the serum of patients with AGII-IV when compared to non-neoplastic samples derived from non-neoplastic patients (NN) ($p > 0.0001$). Quantitative real time PCR (qRT-PCR) of 148 astrocytomas samples (grades I-IV) showed that SAA1 mRNA was significantly higher in Glioblastoma when compared to AGI-III and NN samples ($p < 0.0001$). Immunohistochemistry analysis revealed cytoplasmic positivity for SAA in Glioblastoma. There was no correlation of SAA1 with clinical end-point of overall survival among Glioblastoma patients. However, it was found a positive correlation between SAA1 and genes involved in tumor progression, such as: HIF1A ($r = 0.50$; $p < 0.00001$), CD163 ($r = 0.52$; $p < 0.00001$), CXCR4 ($r = 0.42$; $p < 0.00001$) and CXCR7 ($r = 0.33$; $p = 0.002$). In conclusions, we show that astrocytoma patients have increased levels of serum SAA and SAA1 is expressed and secreted in Glioblastoma, and its co-expression with tumor-related genes supports its involvement in Glioblastoma angiogenesis and progression [1)].

Gene Expression Profiling Interactive Analysis (GEPIA) database was used to identify prognostic genes; serum amyloid A1 (SAA1) was identified as a critical prognostic gene due to higher SAA1 expression associated with poor overall survival (OS) ($HR = 1.5$, $p < .05$) and poor disease-free survival (DFS) ($HR = 1.9$, $p < .01$). Dataset from The Chinese Glioma Genome Atlas database validated the prognostic value of SAA1 and reported the relationship between SAA1 expression and clinical characteristics, including age, sex, history of relapse, and the status of IDH. Gene set enrichment analysis (GSEA) identified six SAA1-related pathways; the identification of pathways could provide insight into the therapeutic strategies of Glioblastoma. Lastly, the relationship between SAA1 expression and immune infiltration was explored, and the result showed that SAA1 expression negatively correlated with the infiltration level of T cells, and SAA1 expression positively correlated with the infiltration level of Treg cells. The overexpression of SAA1 was associated with poor OS and DFS in Glioblastoma, and the expression of the SAA1 gene may affect the infiltration level of immune cells. Therefore, SAA1 could be a promising prognostic biomarker associated with immune infiltration and a therapeutic target for Glioblastoma [2)].

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1)

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