The correlation and prognostic significance of Foxp3 expression in tumor infiltrating lymphocytes and glioma cells from GBM patients

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Abstract:

As the most malignant high-grade glioma, prognosis for patients with glioblastoma multiforme (GBM) has only a median survival of 15 month, and 88% mortality within 3 years. Forkhead box protein 3 (Foxp3) is considered to be an important gene for thymically derived and naturally occurring regulatory T cells (Tregs), which regulate the immunosuppressive response. Recent studies described the expression of Foxp3 in several tumor cells for providing the possibility of effector T-cell evasion. The present work was to investigate its impact in glioblastoma multiforme (GBM) patients. We isolated Tregs from infiltrating lymphocytes (TILs) of GBM by FACS analysis. Then, we analyzed the expression of key molecules of Treg function in lymphocytes and tumor cells and correlate with the DC-therapy response of the corresponding patient. Both Tregs and tumor cells express 3 different isoforms of the FOXP3 gene by alternative splicing, one of which represents a naturally occurring dominant negative version of the Foxp3 protein. The differential expression level of Foxp3 isoforms may constitute a potent prognosis factor for GBM patients. Tregs may limit DC-therapy against GBM, while the differential expression of Foxp3 isoforms could provide a basis for the evaluation of the effectiveness of DC-therapy. Functional abrogation of Foxp3 by tuning the splicing preference to its dominant negative isoform may offer an attractive window to inhibit Treg activity.