FOXP3

FOXP3 (forkhead box P3), also known as scurfin, is a protein involved in immune system responses.

A member of the FOX protein family, FOXP3 appears to function as a master regulator of the regulatory pathway in the development and function of regulatory T cells.

Regulatory T cells generally turn the immune response down. In cancer, an excess of regulatory T cell activity can prevent the immune system from destroying cancer cells. In autoimmune disease, a deficiency of regulatory T cell activity can allow other autoimmune cells to attack the body's own tissues.

Foxp3+ regulatory T cells (Treg) play an important part in the glioma immunosuppression microenvironment. This study analyzed the effect of Foxsp3 on the immune microenvironment and constructed a Foxp3-related immune prognostic signature (IPS)for predicting prognosis in glioblastoma multiforme (Glioblastoma). Immunohistochemistry (IHC) staining for Foxp3 was performed in 72 high-grade glioma specimens. RNA-seq data from 152 Glioblastoma samples were obtained from The Cancer Genome Atlas database (TCGA) and divided into two groups, Foxp3 High (Foxp3_H) and Foxp3 Low (Foxp3_L), based on Foxp3 expression. We systematically analyzed the influence of Foxp3 on the immune microenvironment. Least Absolute Shrinkage and Selection Operator (LASSO) Cox analysis was conducted for immune-related genes that were differentially expressed between Foxp3_H and Foxp3_L Glioblastoma patients. We found a differential expression of Foxp3 in high-grade glioma tissues. The presence of Foxp3 was significantly associated with poor OS. From the four-gene IPS developed, Glioblastoma patients were stratified into low-risk and high-risk groups in both the training set and validation sets. Furthermore, we developed a novel nomogram to evaluate the overall survival in Glioblastoma patients. This study offers innovative insights into the Glioblastoma immune microenvironment and these findings contribute to individualized treatment and improvement in the prognosis for Glioblastoma patients [1)].

In a study of Zhang et al. from the Department of Neurosurgery, General Hospital of Shenyang Military, the frequency and function of regulatory T cells in IA patients were examined. The frequency of Foxp3+ Treg cells was significantly lower in IA patients than in healthy controls. This downregulation was only specific to the Treg subset of CD4+ T cells, as the frequency of total CD4+ T cell was increased in IA patients. Subsequently, we found that the expressions of Treg-associated molecules, including Foxp3, CTLA-4, TGF-β, and IL-10, were significantly lower in Foxp3+ Treg cells from IA patients than in Foxp3+ Treg cells from healthy controls. In both healthy controls and IA patients, Foxp3+ Treg cells were distinguished into a more potent Tim-3+ subset and a less potent Tim-3- subset. The Tim-3+ subset of Foxp3+ Treg cells was significantly reduced in IA patients. Signaling via IL-2, IL-7, IL-15 and IL-21 was shown to promote Tim-3 upregulation in CD4+ and CD8+ T cells. Interestingly, we found that Tim-3 could be upregulated in Treg cells via the same mechanism, but compared to the Treg cells from healthy controls, the Treg cells from IA patients presented defects in Tim-3 upregulation upon cytokine stimulation. Together, our results demonstrated that Foxp3+ Treg cells in IA patients presented reduced function, which was associated with a defect in Tim-3 upregulation [2)].

1)

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2)
Zhang HF, Liang GB, Zhao MG, Zhao GF, Luo YH. Patients with intracranial aneurysms presented defects in regulatory T cells, which were associated with impairment in Tim-3 upregulation. Int Immunopharmacol. 2018 Sep 19;64:350-355. doi: 10.1016/j.intimp.2018.09.020. [Epub ahead of print] PubMed PMID: 30243071.