A Multi-Omics Analysis of Effector and Resting Treg Cells in Pan-Cancer

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Abstract:

Regulatory T cells (Tregs) are critical for maintaining the stability of the immune system and facilitating tumor escape through various mechanisms. Resting T cells are involved in cell-mediated immunity and remain in a resting state until stimulated, while effector T cells promote immune responses. Here, we investigated the roles of two gene signatures, one for resting Tregs (FOXP3 and IL2RA) and another for effector Tregs (FOXP3, CTLA-4, CCR8 and TNFRSF9) in pan-cancer. Using data from The Cancer Genome Atlas (TCGA), The Cancer Proteome Atlas (TCPA) and Gene Expression Omnibus (GEO), we focused on the expression profile of the two signatures, the existence of single nucleotide variants (SNVs) and copy number variants (CNVs), methylation, infiltration of immune cells in the tumor and sensitivity to different drugs. Our analysis revealed that both signatures are differentially expressed across different cancer types, and correlate with patient survival. Furthermore, both types of Tregs

influence important pathways in cancer development and progression, like apoptosis, epithelial-to-mesenchymal transition (EMT) and the DNA damage pathway. Moreover, a positive correlation was highlighted between the expression of gene markers in both resting and effector Tregs and immune cell infiltration in adrenocortical carcinoma, while mutations in both signatures correlated with enrichment of specific immune cells, mainly in skin melanoma and endometrial cancer. In addition, we reveal the existence of widespread CNVs and hypomethylation affecting both Treg signatures in most cancer types. Last, we identified a few correlations between the expression of CCR8 and TNFRSF9 and sensitivity to several drugs, including COL-3, Chlorambucil and GSK1070916, in pan-cancer. Overall, these findings highlight new evidence that both Treg signatures are crucial regulators of cancer progression, providing potential clinical outcomes for cancer therapy.

Keywords:

Regulatory T cells (tregs), Effector tregs, Resting tregs, FOXP3, IL2RA, CTLA-4, CCR8, TNFRSF9, Pan-cancer analysis, Immune infiltration, Gene expression, Tumor microenvironment, Drug sensitivity.