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Quantitative DNA methylation analysis of FOXP3 as a new method for counting regulatory T cells in peripheral blood and solid tissue.

Wieczorek G, Asemissen A, Model F, Turbachova I, Floess S, Liebenberg V, Baron U, Stauch D, Kotsch K, Pratschke J, Hamann A, Loddenkemper C, Stein H, Volk HD, Hoffmüller U, Grützkau A, Mustea A, Huehn J, Scheibenbogen C, Olek S.

Source

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Abstract

Regulatory T-cells (Treg) have been the focus of immunologic research due to their role in establishing tolerance for harmless antigens versus allowing immune responses against foes. Increased Treg frequencies measured by mRNA expression or protein synthesis of the Treg marker FOXP3 were found in various cancers, indicating that dysregulation of Treg levels contributes to tumor establishment. Furthermore, they constitute a key target of immunomodulatory therapies in cancer as well as transplantation settings. One core obstacle for understanding the role of Treg, thus far, is the inability of FOXP3 mRNA or protein detection methods to differentiate between Treg and activated T cells. These difficulties are aggravated by the technical demands of sample logistics and processing. Based on Treg-specific DNA demethylation within the FOXP3 locus, we present a novel method for monitoring Treg in human peripheral blood and solid tissues. We found that Treg numbers are significantly increased in the peripheral blood of patients with interleukin 2-treated melanoma and in formalin-fixed tissue from patients with lung and colon carcinomas. Conversely, we show that immunosuppressive therapy including therapeutic antibodies leads to a significant reduction of Treg from the peripheral blood of transplantation patients. In addition, Treg numbers are predictively elevated in the peripheral blood of patients with various solid tumors. Although our data generally correspond to data obtained with gene expression and protein-based methods, the results are less fluctuating and more specific to Treg. The assay presented here measures Treg robustly in blood and solid tissues regardless of conservation levels, promising fast screening of Treg in various clinical settings.

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