Tnf-α negatively regulates Th2 differentiation in humans

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Abstract

TNF-α is a pleotropic cytokine with multiple physiological functions and is mainly produced from monocytes, macrophages, DCs and T-cells. Along with its physiological functions TNF-α is also a therapeutic target in rheumatoid arthritis, cerebral malaria, sepsis, IBD and psoriasis. However its role in T helper cell differentiation and homeostasis in the above diseases is unclear. In this study we show that TNF-α selectively inhibits the differentiation of human Th2 cells without affecting Th1 and Th17. TNF-α decreased the ROS generation thereby lowered the Erk1/2 phosphorylation in differentiating naïve Tcells thereby down modulated the IL4 synthesis. Whereas cells treated with Anti TNF-α has shown completely opposite effect. Consequently increased TNF-α in T2DM and RA may account for the lowered Th2 differentiation and their increased AICD sensitivity thus exacerbating pre-existing inflammation.

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