Thymus-derived regulatory T cells and conventional CD4+ T cells show distinct metabolic features upon TCR activation

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1. Introduction

In a healthy immune response there is a dynamic balance between opposing activities of two T cell types: conventional T cells (Tconv) and regulatory T cells (Treg). In contrast, immune related diseases are often characterized by a disbalance between these cell types. Low numbers of Tregs can cause auto-immune diseases, while high numbers of Tregs can impede anti-tumor immunity.

Upon activation, T cells must proliferate extremely fast and this places unique demands on their metabolism. However, whereas proliferation of Tconvs rely on the mTORC1 pathway, thymic derived Treg (tTreg) can proliferate in an mTOR independent fashion. Our goal is to investigate these differences in metabolism between Tconvs and Tregs.

In addition, T cell activation is a multiple-signal process. Signal 1 is via T cell receptor (CD3) and signal 2 is an integration of co-stimulatory and co-inhibitory input directing the immune response.

In this study addition of a co-stimulatory signal via CD28 vs CD3 only stimulation was also investigated, how this affects the metabolism in Tconv and tTreg.

2. Approach

CD4+ Tconv and tTreg were sorted and expanded, and state-of-the-art LC/MS was used to map metabolic differences between resting and CD3 only or CD3/28-activated Tconv and tTreg.

3. Results

Our data reveal specific differences between activated Tconv and tTreg in several metabolic pathways, including the glycolysis, amino acid, and nucleotide metabolism. Tconv seem to undergo a larger metabolic switch than tTreg, in particular with CD3/28 co-stimulation.

4. Discussion

Further investigation of the emerging differences between Tconv and Treg may aid in the identification of metabolic targets that can selectively modulate T cell activity.