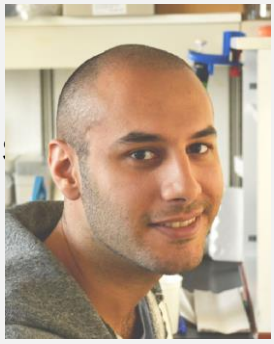
ImmunoTools *special* Award 2014



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Expanding regulatory T-cells via metabolic intervention

Interactions between immune system and metabolic processes have been suggested for decades. However, our understanding of this interplay has increased dramatically over the past years. Immune reactivity was found to be profoundly altered in states of metabolic imbalance and further to promote the pathomechanisms leading to diseases as diabetes mellitus or autoimmunity. A broad range of cells have been implicated in this process, whereas the most important players appear to be macrophages and T-cells.

As it is becoming evident that metabolic deregulation of immune cells is a crucial factor in the pathogenesis of metabolic disease, manipulation of these processes arises as a new option in prevention and treatment. Particularly the mode of energy utilization of immune cells has been demonstrated to lead to alterations in their effector mechanisms. While the preferential utilization of glucose has been implicated in the generation a pro-inflammatory effector phenotype, utilization of fatty acids (i.e. oxidative phosphorylation) has been shown to be used by regulatory immune cells. This process has been demonstrated to be crucial for the polarization of macrophages (M1 utilizing glucose while M2 fatty acids) and T-cells (Th1,Th2,Th17 utilizing glucose whereas Treg depend on fatty acid metabolism) (for review see [1]). Furthermore, it has been recently shown that not only regulatory T-cells have a fundamentally different way of utilizing energy, but the enforcement of a metabolism depending on oxidative phosphorylation skews cells towards a regulatory phenotype [2].

The addition of fatty acids leads to enhanced oxidative phosphorylation and ultimately to the generation of more regulatory T-cells[2]. We hypothesize that inhibition of glycolysis might lead to the same effects via a distinct and more applicable mechanism. Thus, in this study we are analyzing the role of glycolysis inhibition on the polarization of T-cells during activation. To this end, isolated CD4-positive T-helper cells are stimulated and incubated with different glycolysis inhibitors. Afterwards, they are characterized for their surface marker profile and functional capacity. Additionally, we aim to characterize the modulating effects within different polarization protocols (additional incubation with Th1/Th2/Th17/Treg inducing cytokines). Furthermore, we will analyze the effects of these glycolysis inhibiting agents on the T-helper cell subsets in vivo.

As stated above a broad range of antibodies and cytokines is necessary to accurately characterize the induced alterations on the one hand and to perform the polarization protocols on the other. Therefore, the reagents offered in the ImmunoTools award would be extraordinary helpful in the performance of this study.

References:

1. O'Neill LAJ, Hardie DG (2013) Metabolism of inflammation limited by AMPK and pseudo-starvation. Nature 493: 346–355. doi:10.1038/nature11862.
2. Michalek RD, Gerriets VA, Jacobs SR, Macintyre AN, MacIver NJ, et al. (2011) Cutting edge: distinct glycolytic and lipid oxidative metabolic programs are essential for effector and regulatory CD4+ T cell subsets. J Immunol Baltim Md 1950 186: 3299–3303. doi:10.4049/jimmunol.1003613.

ImmunoTools *special* AWARD for **Guido Gualdoni** includes 25 reagents

FITC - conjugated anti-mouse CD4, CD8a, CD11b, CD45, CD62L, isotpye control IgG2b,

PE - conjugated anti-mouse CD4, isotpye control IgG2b,

APC -conjugated anti-mouse CD3e, CD19, CD45, isotpye control IgG2b,

recombinant mouse cytokines rm GM-CSF, rm IFNgamma, rm IL-2, rmIL-3, rm IL-4, rm IL-6, rm IL-10, rm IL-13, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-20, rm IL-22

DETAILS