Immunological Self-tolerance and Metabolism

Over the past decade, “immunometabolism” has become one of the most exciting areas of translational research. Metabolic processes regulate immune cell responses in healthy individuals as well as during infection, cancer and autoimmunity.

In this context, the main research topic of our Group of Immunology and ImmuneMetabolism, at the IEOS-CNR, is the study of the cellular and molecular mechanisms governing the immune self-tolerance and the interactions between the metabolic/nutritional status and the immune response.

Starting from the observation that metabolic status influences immunological tolerance, we study the functional alterations of regulatory T cells (Treg), a cellular subset with a central role in the control of immunological tolerance, in different models of autoimmune and inflammatory diseases, such as multiple sclerosis (MS), type 1 diabetes (T1D) and chronic obstructive pulmonary disease (COPD) (1, 2). In the last few years, we identified the mammalian target of rapamycin (mTOR) as a key “metabolic” sensor pathway that controls Treg cell homeostasis, expansion and function (3). Our published evidence also revealed that mTOR is dysregulated in Treg cells from MS patients and this is associated with an altered expression of the lineage-specific transcription factor Foxp3 and impaired Treg cell proliferation (4).

Our group also defined the intracellular metabolic asset of human Treg cells (5), identifying the glycolytic pathway as the main molecular program needed for the generation of functional Tregs cells, through the induction of a specific splicing form of FoxP3 (Foxp3-Exon2), crucial for Treg cell suppressive activity. Altered glucose metabolism and Foxp3-E2 expression associated with defective function of Treg cells from both MS subjects and T1D children (6).

More recently we became interested in the study of novel immunometabolic therapeutic approaches, such as the calorie restriction (CR) for the treatment of autoimmunity and for the control of infection susceptibility. Indeed, recent data from our laboratory revealed that manipulation of nutritional status, through CR, protects from pulmonary mycobacterium tuberculosis (MTB) infection, inducing an immunometabolic reprogramming and enhancing intracellular MTB killing by immune cells.

Taken together our results reveal how metabolism impinges on immune cells and specifically on Treg cell fitness and plasticity and will be therefore instrumental to foresee and exploit novel Treg-specific therapeutic strategies, based on their metabolic manipulation, to treat autoimmune and inflammatory disorders.

Referenze:


**Parole chiave:**
immunological self-tolerance, metabolism, Treg cells.

**Contatti:**
e-mail Prof. Giuseppe Matarese, Email: giuseppe.matarese@cnr.it or giuseppe.matarese@unina.it
Web: www.matareselab.it

**Altro:**