Type I interferon is critical for the homeostasis and functional maturation of type 3 T cells

Agerholm, Rasmus; Kadekar, Darshana Dattatraya; Rizk, John; Bekiaris, Vasileios

Published in:
Scandinavian Journal of Immunology

Publication date:
2017

Document Version
Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.
A-31311

Th2 cell metabolism

Julian M. Stark, Chris Tibbitt, Ganna Oliynyk, Marie Arsenian Henriksson & Jonathan M. Coquet
Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden

T helper cells undergo rapid proliferation upon activation and differentiate into cells producing high levels of cytokines. This requires large amounts of energy. Metabolic pathways such as glycolysis are important for the development of functional T helper cell subsets, but molecules in the glycolytic pathway have also been found to have targeted effects on T helper cell effector functions. Type 2 T helper cells are characterized by their production of IL-5 and IL-13 and are involved in immune responses to parasites, and in allergies. The role of metabolism for the development and function of Th2 cells is not very well understood. In this study, we aim to determine the levels of glycolysis of in vitro generated Th2 cells and to investigate the role of glycolysis for the effector function of Th2 cells.

We used the Seahorse XF Analyzer to measure levels of glycolysis. We used both in vitro differentiated T helper cells and cells from inflamed mice lungs. Expression of cytokines and metabolic markers was assessed by flow cytometry.

We show that in vitro generated Th2 cells require active glycolysis for the production of IL-5 and IL-13 as addition of 2-DG impaired secretion of these cytokines. Th2 cells were also more glycolytic and possessed greater glycolytic capacity than other in vitro generated T helper cell subsets. We believe that this link between glycolysis and Th2 function and a general better understanding of Th2 metabolism will lead to novel strategies for the treatment of asthma and allergies in the future.

A-31312

Identification and functional characterization of non-human primate myeloid-derived suppressor cells during vaccination

Ang Lin1,2, Frank Liang1,2, Elizabeth A. Thompson1,2, Maria Vono1,2, Sebastian Ols1,2, Gustaf Lindgren1,2, Hugh Salter3 & Karin Lore4,2
1Department of Medicine Solna, Immunology and Allergy Unit, Karolinska Institutet, Stockholm, Sweden, 2Center for Molecular Medicine, Stockholm, Sweden, and 3Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

A number of conditions associated with chronic inflammation, autoimmune disease and cancer leads to accumulation of myeloid-derived suppressor cells (MDSCs) that play a considerable role in regulating T cell responses. Whether MDSCs increase and influence T cell responses in temporary inflammation like after vaccine administration is unknown. Utilizing a nonhuman primate model, we demonstrate that the two main subsets monocytic (M)-MDSCs and polymorphonuclear (PMN)-MDSCs can be detected using several of the markers used in humans. However, while rhesus M-MDSCs lacked expression of CD33, PMN-MDSCs were identified as CD33+ low-density neutrophils. Importantly, both M-MDSCs and PMN-MDSCs showed suppression of T cell proliferation in vitro. The frequency of circulating MDSCs rapidly and transiently increased 24 hrs after vaccine administration. M-MDSCs infiltrated the vaccine injection site but not vaccine-draining lymph nodes. In line with this, the expression of genes relevant to MDSCs such as arginase-1, IDO1, PD-L1 and IL-10 was upregulated at the vaccine injection site. MDSCs may therefore play an important role in locally maintaining immune balance to prevent potential excessive immune activation and inflammation caused by vaccine exposure.

Keywords: Myeloid-Derived Suppressor Cells, Low-Density Neutrophils, CD33, Vaccination, Nonhuman Primates

A-31314

Type I interferon is critical for the homeostasis and functional maturation of type 3 γδ T cells

Rasmus Agerholm, Darshana Kadekar, John Rizk & Vasileios Bekiaris
Technical University of Denmark (DTU), Veterinary Institute, Section for Immunology & Vaccinology, Kemitorvet, Kgs Lyngby, Denmark

Type I IFN (IFN-I) is highly expressed during viral infection and many autoimmune pathologies such as SLE and psoriasis. In addition, IFN-I is important to maintain the homeostasis of a number of different immune populations. Our aim was to identify whether IFN-I regulates type 3 γδ T (γδT3) cells. We found that IFNαβ inhibits the activation of γδT3 cells following treatment with cytokines such as IL-23 and IL-17 and abrogates their ability to produce IL-17 during viral infection. Despite this inhibitory role, γδT3 cells that are deficient in type 1 IFN receptor (IFNAR) signaling display anergic behavior. Such γδT3 anergy is characterized by failure to induce skin inflammation and unresponsiveness to cytokine stimuli. Moreover, IFNAR deficient mice display deregulated γδT3 homeostasis due to a neonatal maturation defect. In conclusion, our data show that tonic type I IFN signaling during neonatal and adult life is required for the full maturation and pro-inflammatory function of γδT3 cells, however acute type I IFN production during viral infection acts as a γδT3 inhibitor.