Adaptive immunity (T cells and B cells) in rheumatic diseases

Objectives: To determine the incidence of ADAb against the anti-TNF agents IFX and ADA, and to evaluate the therapeutic response to these agents in patients with rheumatic diseases. The study included patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA) treated with IFX or ADA as a first-line treatment for at least six months. ADAb and trough levels were measured at the time of sampling.

Results: Fifty patients were included, 17 RA and 33 SpA. ADAb were positive in 39% of SpA and 35% of RA. They were positive in 40% of cases for IFX and 25% for ADA. The presence of ADAb was negatively related to the trough levels noted on the therapeutic response at the time of sampling. However, the presence of ADAb was related to a higher activity of SpA six months after the sampling (p=0.05). Factors that were related to ADAb formation were a high BMI in RA and a longer duration of evolution of RA.

Conclusion: The presence of ADAb and low trough levels seem to not affect the therapeutic response at the time of sampling (p=0.05). Factors that were related to ADAb formation were a high BMI in RA (p=0.05) and a longer duration of evolution of RA (p=0.03).

Disclosure of Interests: None declared

IMPACT OF METABOLIC CHANGES DURING AGING ON HUMAN EX VIVO NAÏVE AND MEMORY CD4+ T CELL FUNCTION

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Background: Age-related dysfunction in immune cells (immunosenescence), such as T cell dysfunction, may contribute to the development of rheumatoid arthritis (RA). In aged people, senescent T cells tend to produce low amounts of pro-inflammatory cytokines, leading to low-grade inflammation. However, cellular metabolism modulates effector functions such as cytokine production and proliferation in T cells by providing energy and building blocks. Metabolically, naïve and memory CD4+ T cells are relatively quiescent immune cells. Currently, the metabolic phenotype of naïve and memory CD4+ T cells and how metabolism affects functions of naïve and memory CD4+ T cells in aged people are not well understood.

Objectives: To analyse the differences in the metabolic phenotype of peripheral naïve and memory CD4+ T cells in young and aged healthy donors to explore fundamental processes of immune-aging in the pathogenesis of RA.

Methods: Naïve and memory CD4+ T cells were sorted by flow cytometry and molecular identity was further determined by transcriptional analysis. Additional functional assay was also performed to explore those distinct effector B cells.

Results: Functional studies were performed on both naïve and memory CD4+ T cells. Naïve CD4+ T cells from young donors had higher basal glycolysis, and memory CD4+ T cells from young donors had higher basal glycolysis, and compensatory glycolysis as well as basal OCR and spare respiratory capacity than naïve CD4+ T cells. Memory CD4+ T cells from young donors had higher basal glycolysis, and compensatory glycolysis than aged donors, but lower ratio of basal mitoOCR/ glycolysis. Although we did not observe differences in intercellular cytokine expression measured by flow cytometry after 5h stimulation of memory CD4+ T cells, we determined a significant higher amount of secreted IL-6, IL-9, IF-10, monocyte chemotactic and activating factor in the supernatant of memory CD4+ T cells from aged donors as compared to those from young donors. Cell division index, proliferation, percentage of divided cell, and Ki-67 expression after 3 and 4 days by flow cytometry.

Conclusion: Here, we demonstrate a higher basal glycolysis, basal OCR, mitochondrial and glycolytic capacity of human ex vivo memory CD4+ T cells as compared to naïve T cells. A decrease of basal glycolysis, compensatory glycolysis in memory CD4+ T cells of aged people which results in an enhanced cytokine expression and secretion was measured by flow cytometry and multiplex assay. Finally, TCR-stimulated memory CD4+ T cell proliferation was determined using CFSE and Ki-67 after 3 days and 4 days by flow cytometry.

Disclosure of Interests: None declared

STUDY OF FUNCTIONAL ORIENTATION OF B CELLS IN PHYSIOLOGY AND SJÖGREN’S SYNDROME

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Background: Sjögren’s syndrome (SS) is a chronic systemic autoimmune disease characterized by mouth and eye dryness, due to irreversible destruction of glandular tissue by infiltrated lymphocytes. It is now well established that B cells play a key role in the pathophysiology of SS. Indeed, B cells exhibit various signs of hyperactivity and produce excessive amounts of pro-inflammatory cytokines and immunoglobulins (lg), especially IgG type-antibodies (Abs) (Kroese et al., 2014). Currently, it is suggested that the interleukin (IL)-21 (Wang et al., 2018) and IFNs (Yao et al., 2013), promote the generation of autoreactive IgG-producing plasma cells (PC). On the other side, some studies highlight the protective role of IgM producing cells in autoimmunity through enhanced effectorcytosis and immune-regulatory properties (Ordenstein and Notley, 2010).

Objectives: To study the influence of IL21 and IFNs on the B cell differentiation and the subsequent functional responses of the cells according to their maturation stage. Moreover, this will also enable a further understanding of the contribution of these cytokines to the pathogenesis of SS.

Methods: We established in vitro models to study the differentiation of different B cell subsets in a T-independent (TI) and T-dependent (TD) manner, under different cytokine stimulations. naïve, switched memory and CD27-negative memory B cells were isolated from peripheral blood of healthy controls (HC) and SS patients and thereby cultured in different conditions. After three days of culture, the expression of surface markers and transcription factors was analysed by flow cytometry and molecular identity was further determined by transcriptional analysis. Additional functional assay was also performed to measure Abs and cytokine secretion.

Results: First results on HC suggest that switched memory B cells differentiate into IgG and IgA-secreting plasmablasts (PB), when stimulated in a T1 manner. This process is highly increased in presence of IFNs. Unswitched memory B cells mostly become PB able to secrete IgM and IL10. IL21 and IFNs oppose distinct effector functions. IL21 promote activation of B cells with an upregulation of the surface marker CD11c and T-bet transcription factor. Transcriptomic studies are still in progress to further define the molecular profile of those distinct effector B cells.