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

IMMUNOGENICITY OF TNF ALPHA ANTAGONISTS IN RHEUMATIC INFLAMMATORY DISEASES : IMPACT ON CLINICAL RESPONSE
Selma Bouden1, Liila Laadhar2, Imen Ayadi2, Mariam Saleml1, 1 Rabta hospital, tunis, Tunisia; 2 Rabta hospital, tunis, Tunisia

Background: One of the mechanisms implicated in the loss of response to TNF alpha antagonists in rheumatic inflammatory diseases is the formation of antibodies against these drugs (anti-drug antibodies: ADA).

Objectives: The objective of our study was to determine the incidence of ADA and anti-Infliximab (IFX) and anti Adalimumab (ADA) and to evaluate the therapeutic impact of the presence of ADA, the rate of ADA and trough serum concentration of the drug at the time of sampling and six months later.

Methods: A longitudinal, prospective and multicenter study was conducted including patients with rheumatoid arthritis (RA) or spondyloarthritides (SpA) treated with IFX or ADA as a first biotherapy for at least six months. ADAbs and trough levels were measured. The evaluation of the therapeutic response was made at the time of sampling and six months later.

Results: Fifty patients were included (17 RA and 33 SpA). ADAbs 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 ADA was negatively related to the trough levels of IFX and ADA during RA (p=0.01 and p<0.0001) and SpA (p<0.01 and p<0.0001). For the two pathologies, no impact of the presence of ADA, the rate of ADA on the trough levels was noted on the therapeutic response at the time of sampling. However, the presence of ADA was related to a higher activity of SpA six months after the sampling (p=0.05). Factors that were related to ADA formation were a high BMI in RA (p=0.05) and a longer duration of evolution of RA (p=0.03).

Conclusion: The presence of ADA and low trough levels seem to not affect the therapeutic response in patients on TNF alpha antagonists. Other tracks than immunogenicity should be investigated to explain the loss of response to these biotherapies.

Disclosure of Interests: None declared

AB0023 IMPACT OF METABOLIC CHANGES DURING AGING ON HUMAN EX VIVO NAÏVE AND MEMORY CD4+ T CELL FUNCTION
Yuling Chen1,2, Pelle Löwe1,2, Hao Wu3, Frank Buttgeriet1,2, Timo Gaber3,2
1Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Rheumatology and Clinical Immunology, Berlin, Germany; 2German Rheumatism Research Centre (DRFZ) Berlin, a Leibniz Institute, Berlin, Germany; 3Charité – Universitätsmedizin Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Gastroenterology, Infectiology and Rheumatology, Berlin, Germany

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 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: Therefore, we analysed 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: 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, unswitched memory and CD27-negative memory B cells were isolated from peripheral blood of healthy controls (HC) and SS patients and thereby cultured in those different conditions.

Results: First results on HC suggest that switched memory B cells differentiate into IgG and IgA-secreting plasmablasts (PB), when stimulated in a TI manner. This process is highly increased in presence of IFNs. Unswitched memory B cells mostly become PB able to secrete IgG and IL10. IL21 and IFNα 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 in progress to further define the molecular profile of those distinct effector B cells.

Preliminary results on SS patients suggest that B cell differentiation is altered with a biased ratio between activated cells and PB.

Conclusion: This work will allow us a better understanding of the heterogeneity of the distinct effector B cells and their involvement in SS pathogenesis.

Disclosure of Interests: None declared

AB0024 STUDY OF FUNCTIONAL ORIENTATION OF B CELLS IN PHYSIOLOGY AND SJÖGREN’S SYNDROME
Marina Boudigu1, Alexis Grasseau1, Nedra Chriti1, Divi Cornecl1,2, Jacques-Olivier Pers1,2, Sophie Hillon1, Laetitia Le Pottier1, 1 Univ Brest, Inserm, UMR1227, Lymphocytes B et Autoimmunité, Brest, France, Brest, France; 2 CHU de Brest, Brest, France, Brest, France

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 physiopathology 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 immunoglobulins (Ig), especially IgG type-antibodies (Ab) (Kroese et al., 2014). Currently, it is suggested that the interleukin (IL)-21 (Wang et al., 2018) and immunoglobulins (Ig), especially IgG type-antibodies (Abs) (Kroese et al., 2014). Currently, it is suggested that the interleukin (IL)-21 (Wang et al., 2018) and immunoglobulins (Ig), especially IgG type-antibodies (Abs) (Kroese et al., 2014).

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, unswitched memory and CD27-negative memory B cells were isolated from peripheral blood of healthy controls (HC) and SS patients and thereby cultured in those different conditions.

Results: First results on HC suggest that switched memory B cells differentiate into IgG and IgA-secreting plasmablasts (PB), when stimulated in a TI manner. This process is highly increased in presence of IFNs. Unswitched memory B cells mostly become PB able to secrete IgG and IL10. IL21 and IFNα 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 in progress to further define the molecular profile of those distinct effector B cells.

Preliminary results on SS patients suggest that B cell differentiation is altered with a biased ratio between activated cells and PB.

Conclusion: This work will allow us a better understanding of the heterogeneity of the distinct effector B cells and their involvement in SS pathogenesis.

Disclosure of Interests: None declared

REFERENCES