AB0030
INCREASED CIRCULATING CD19+CD224HICD38HI REGULATORY B CELLS ARE BIOMARKERS OF RESPONSE TO METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS
P. Forteza-Gordo1, A. Villalba1,2, L. Nuño1,2, M. J. Santos-Bornez1,2, D. Peiteado1,2, I. Monjo1,2, A. Puig-Kröger3, P. Sanchez-Mateos2, E. Martin-Mola4, A. Balsa1,2, M. E. Miranda-Carus1,2,1
1University Hospital La Paz, Rheumatology, Madrid, Spain; 2Fundación Para La Investigación Biomédica Del Hospital Universitario La Paz, Madrid, Spain; 3Hospital Gregorio Marañón, Immunono- oncology, Madrid, Spain; 4-medical, Madrid, Spain

AB0031
T HELPER 17 CELLS WERE SIGNIFICANTLY DECREASED BY MITOCHONDRIAL ELECTRON TRANSPORT COMPLEX INHIBITOR IN PATIENTS WITH RHEUMATOID ARTHRITIS
H. R. Lee1,2, J. S. Yoo1, J. Kim1, I. S. Yoo1, C. K. Park3, S. W. Kang3,1
1Chungnam National University, Daejeon, Korea, Rep. of (South Korea); 2Chungnam National University Hospital, Daejeon, Korea, Rep. of (South Korea)

Background: Reactive oxygen species (ROS) and T helper 17 (TH17) cells have been known to play an important role in the pathogenesis of rheumatoid arthritis (RA). However, the interrelationship between ROS and TH17 remains unclear in RA.

Objectives: To explore whether ROS affect TH17 cells in peripheral blood mononuclear cells (PBMC) of RA patients, we analyzed ROS expressions among T cell subsets following treatment with mitochondrial electron transport chain complex inhibitors.

Methods: Blood samples were collected from 40 RA patients and 10 healthy adult volunteers. RA activity was divided according to clinical parameter DAS28. PBMC cells were obtained from the whole blood using lymphocyte separation and medium density gradient centrifugation. Following PBMC were stained with Live/Dead stain dye, cells were incubated with antibodies for CD3, CD4, CD6, and CD25. After fixation and permeabilization, samples were stained with antibodies for FoxP3 and IL-17A. MitoX320 and MitoP3 were used for mitochondrial specific staining.

Results: The frequency of TH17 cells was increased by 4.83 folds in moderate disease activity group (S.1-DAS28>3.2) of RA patients compared to healthy control. Moderate RA activity patients also showed higher ratio of TH17/Treg than healthy control (3.57 folds). All RA patients had elevated expression of mitochondrial specific ROS than healthy control. When PBMC cells were treated with 2.5μM of antimycin A (mitochondrial electron transport chain complex III inhibitor) for 16h, the frequency of TH17 cells was significantly decreased.

Conclusion: The mitochondrial electron transport chain complex III inhibitor markedly downregulated the frequency of TH17 cells in moderate disease activity patients with RA. These findings provide a novel approach to regulate TH17 function in RA through mitochondrial metabolism related ROS production.

References:

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3441

AB0032
ABNORMAL STATUSES OF PERIPHERAL CD4+T CELL SUBSETS IN PATIENTS WITH GOUT AND THEIR CHANGES AFTER RECEIVING COMBINED IMMUNOMODULATORY THERAPY
M. J. Chang1, S. X. Zhang1, L. Zhao1, J. Qiao2, J. Zhang2, M. T. Qiu1, R. Zhao3, Y. L.4, C. Wang4, J. Luo5, G. Y. Liu5, C. Gao5, X. Li4,1
1Shanxi Medical University, Taiyuan, China; 2The Second Hospital of Shanxi Medical University, Taiyuan, China; 3Birmingham and Women’s Hospital, Harvard Medical School, Boston, United States of America

Background: Gout is a chronic systemic inflammatory disease that results from the deposition of monosodium urate crystals in joints and the associated activation of the innate immune system associated with hyperuricemia. As the pathogenesis of gout is still a matter of speculation and debate, accumulating evidence converges on inflammasome activation and immunological dysregulation. However, the detailed statuses of lymphocyte subsets in patients with gout are unknown and influence of immunomodulatory combination therapies on the lymphocyte subsets remain to be clearly evaluated.

Disclose Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.930

References:
Objectives: To evaluate the quantitative statuses of peripheral CD4<sup>+</sup> T subpopulations in patients with gout and further investigate the effects of immunomodulatory combination therapies on those cells.

Methods: Total 247 patients who met the clinical criteria of gout from the American College of Rheumatology and 206 healthy controls (HCs) were enrolled in this retrospective cross-sectional study. Among those patients, 70 follow-up patients donated their peripheral blood after receiving immunomodulatory drugs (e.g., low-dose interleukin-2, rapamycin, metformin, retinoic acid, etc.). The absolute numbers of Th1, Th2, Th17 and Tregs in peripheral CD4<sup>+</sup> T subsets were detected by flow cytometry combined with standard absolute counting beads.

Results: Compared with HCs, the absolute numbers of Th1 and Th17 were evidently increased in gout patients (P<0.001), while the level of Tregs was significantly decreased (P<0.05) (Figure 1). After immunomodulatory combination treatments, there were dramatical increases in a wide variety of CD4<sup>+</sup> T subsets such as Th1, Th17 and Tregs (P<0.05). Interestingly, the increased amount of Tregs was much more than that of other Teffs, leading to the decrease ratios of Teffs/Tregs such as Th2/Tregs, restoring immune homeostasis (Figure 2).

Conclusion: This cross-sectional study clarified the abnormal statuses of CD4<sup>+</sup> T subsets in gout patients, suggesting that CD4<sup>+</sup> T subsets, especially Tregs, might be relevant and play a crucial role in the pathogenesis of gout, thus providing a potential therapeutic target for gout patients. Immunomodulatory combination therapies effectively increase the number of Tregs and may help for gout patients' symptom remission.

**References:**


Acknowledgments: None.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5844

---

**AB0033**

**CHARACTERIZATION OF THE PERIPHERAL B CELL COMPARTMENT IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS**

R. Lorentzen<sup>1</sup>, M. Engesser<sup>1</sup>, R. Voß<sup>1</sup>, A. Troilo<sup>1</sup>, I. Janowska<sup>1</sup>, M. Rizzi<sup>1</sup>, N. Venthoff<sup>1</sup>, J. Thiel<sup>1</sup>, Vasculitis Center Freiburg, Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, Freiburg, Germany

**Background:** Eosinophilic granulomatisis with polyangiitis (EGPA) is a rare form of systemic vasculitis, which is characterized by bronchial asthma, hypereosinophilia, and systemic vasculitis. B-lymphocytes play a key role in EGPA as producers of IgE and anti-neutrophil cytoplasmic antibodies (ANCAs). Indeed, the neutrophils that are targeted by these antibodies are widely described as the mechanism of endothelial damage in this disease. On the other side, the therapeutic response to rituximab in EGPA patients provides evidence for a role of B-cells in the pathogenesis of EGPA. Therefore characterizing B cell subpopulations may help in understanding the disease and the treatment.

**Objectives:** To characterize the peripheral B cell compartment in patients with EGPA and to analyze the in vivo potential of B lymphocytes to class-switch to IgE and to assess in vivo the differential potential of naive B cells of EGPA patients into IgE-secreting plasmablasts.

**Methods:** Clinical characteristics of the patients, including organ involvement and treatment regimen were evaluated. Laboratory work-up included ANCA-status, eosinophils, IgE, IgG, IgA, IgM, and peripheral CD19<sup>+</sup> B-cell count. For immunophenotyping isolated PBMCs were stained with monoclonal or polyclonal antibodies (e.g., low-dose interleukin-2, rapamycin, metformin, retinoic acid, etc). The patients donated their peripheral blood after receiving immunomodulatory drugs in this retrospective cross-sectional study. Among those patients, 70 follow-up patients and 206 healthy controls (HCs) were enrolled.

**Results:** 34 patients with EGPA diagnosed according to ACR and CHC-criteria were included into the study. Ten of these patients were analyzed separately because they received rituximab therapy. Peripheral B cell numbers in EGPA patients were markedly diminished. B cell subpopulation phenotyping showed in average 57.9% naive B cells, 12.5 % marginal zone like B cells and 19.2% switched memory B cells. Plasmablasts constituted in average 1.15% of the peripheral B cell compartment, transitional B cells 2.0%. Interestingly, the expression of BAFF receptor and TACI in the memory B cell subset was significantly decreased in EGPA patients when compared with healthy donors. In vitro assays of isolated B cells from EGPA patients demonstrated an increased proportion of IgE-class-switched B cells after 9 days of culture under IL4 stimulation compared with controls. However, no differences were observed in the phosphorylation of STAT5 and STAT6 after stimulation with IL4 or IL21.

**Conclusion:** In the EGPA-patients we observed markedly diminished B-cells despite of normal lymphocyte counts. B cells showed a reduced expression of BAF-FR and TACI. Class switch to IgE is enhanced in EGPA patients.

**Disclosure of Interests:** None declared

DOI: 10.1136/annrheumdis-2020-eular.5844

---

**AB0034**

**EARLY IMMUNIZATION AGAINST TREATMENT IS ASSOCIATED TO POOR CLINICAL RESPONSE AT 6 MONTHS AND LOW NUMBER OF TRANSITIONAL B CELLS AT BASELINE IN RHEUMATOID ARTHRITIS PATIENTS TREATED BY ADALIMUMAB**

C. Lucas<sup>1</sup>, S. Rodrigues<sup>2</sup>, R. Jean<sup>3</sup>, J. D. Albert<sup>4</sup>, G. Collifer<sup>1</sup>, E. Dumontier<sup>1</sup>, K. Tarte<sup>1</sup>, P. Amé-Thomas<sup>1</sup>, A. Perdriger<sup>1</sup>, 1University Hospital, Rheumatology, Rennes, France; 2INSERM1236, Rennes, France

**Background:** Circulating anti-drug antibodies (ADAs) are detectable proportionately in 33% of adalimumab treated rheumatoid arthritis (RA) patients, often within the first 6 months of therapy<sup>1,2</sup>. Classically, circulating ADAs associate with their specific drugs to form immune complexes, increasing drug clearance, and by this mechanism reducing therapeutic effect<sup>2</sup>. B cell involvement leading to ADAs production is not yet well established.

**Objectives:** To evaluate the anti-drug antibodies (ADAs) in a cohort of RA patients treated with adalimumab and to analyze their clinical response.

**Methods:** Anti-drug antibodies were measured in 128 RA patients treated with adalimumab at baseline and 6 months. The patients were classified into three groups according to their ADA status: ADA positive, ADA negative or ADA positive at 6 months. The correlation between ADA status and clinical response was evaluated. The clinical response was defined according to the European League Against Rheumatism (EULAR) recommendations.

**Results:** Among 128 RA patients, 29 (22.5%) were ADA positive at baseline and 6 (4.7%) at 6 months. The clinical response was better in ADA negative and ADA positive at 6 months patients compared to ADA positive at baseline patients (P<0.05). The proportion of patients without at least a 20% improvement in the American College of Rheumatology (ACR) 20 criteria was significantly higher in ADA positive at baseline patients (P<0.05).

**Conclusion:** Early immunization against treatment is associated to poor clinical response at 6 months and low number of transitional B cells at baseline in rheumatoid arthritis patients treated by adalimumab.

**Disclosure of Interests:** None declared

DOI: 10.1136/annrheumdis-2020-eular.5844