intracellular metabolomics, chromatin immunoprecipitation PCR, ATAC and RNA sequencing, and cytokine production assays. Arteries from GCA patients were evaluated with immunohistochemistry (IHC) to assess immunometabolic activation. Pharmacologic inhibition of immunometabolic changes underlying TI (ie, glycolysis) was evaluated ex vivo as a therapeutic strategy to suppress cytokine production.

**Results:** GCA monocytes exhibited hallmark molecular features of TI. Specifically, these included typical immunometabolic changes (eg, increased glycolysis and glutaminolysis through the TCA cycle), epigenetic changes promoting transcription of genes governing pro-inflammatory activation, and enhanced IL-6 production upon inflammatory challenge. IHC revealed that GCA lesions are highly glycolytic microenvironments, and pharmacologic inhibition of glycolysis with 2-deoxy-glucose effectively dampened IL-6 production.

**Conclusion:** This study reveals the deleterious potential of maladaptive TI in the pathogenesis of GCA, and the therapeutic potential of inhibiting TI for the treatment of this condition.

**Acknowledgements:** This study was supported by the Foundation for Research in Rheumatology (FOREUM Career Award 2020 to GC). GC is also supported by AIRC under MFG 2018 (ID. 22136 project – P. G. Giulio Cavalli); EHA (European Haematology Association Physician Scientist Grant 2021); Italian Ministry of Health (GR-2018-12366385); SIMI (Italian Society of Internal Medicine, G. Licata Award 2021).

**Disclosure of Interests:** Elenonora Conti: None declared, Ivan Merelli: None declared, Davide Stefanoni: None declared, Alessandro Tomelleri: None declared, Corrado Campochiaro: None declared, Elena Baldissera: None declared, Jorge Dominguez Andres: None declared, Marco Matucci-Cerinic: None declared, Angelo DiAlessandro: None declared, Lorenzo Dagna: ‘SANOBI, NOVARTIS, SOBI, Mihai Netea: None declared, Raffaele Molteni: None declared, Giulio Cavalli: None declared.

**DOI:** 10.1136/annrheumdis-2022-eular.1540

---

**1H-NMR BASED METABOLIC PROFILE OF PATIENTS WITH GIANT CELL ARTERITIS AND POLYMALGIA RHEUMATICA IN ACTIVE AND INACTIVE DISEASE STATE**

O. Antypouloou, M. Karagiannakou, D. Palamidas, D. Benaki, K. Tsezou, P. Vlachosianopoulos, E. Mikes, A. Tzioulas, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece; School of Pharmacy, National and Kapodistrian University of Athens, Department of Pharmaceutical Chemistry, Athens, Greece

**Background:** Giant cell arteritis (GCA) is the most common form of systemic vasculitis in the elderly. The disease is characterized by a remarkable heterogeneity in terms of clinical picture, histologic pattern of the affected vessels, pathogenetic mechanisms and treatment selection strategies. Approximately half of GCA patients present with polymyalgia rheumatica (PMR), while 20% of PMR patients will develop GCA during follow-up. Organ or life-threatening complications of GCA, include vision loss, strokes, aneurysm formation and accelerated atherosclerosis. The clinical heterogeneity along with the increased relapse rate, even under treatment and the fact that ESRI and C-Reactive Protein are the only laboratory tools for the assessment of active disease suggest that the definition of new biomarkers with diagnostic, prognostic and predictive value is an unmet need (1). Among the high throughput approaches towards this direction, 1H NMR spectra of serum samples provides a direct, untargeted, and holistic metabolic profile offering a wealth of information that could be proved useful to discover outcome tools for the management of the disease (2).

**Objectives:** 1. To characterize and compare the metabolic profile of GCA/PMR serum samples, as captured in 1H NMR spectra, in 3-time points: diagnosis, 1 and 6 months of treatment with steroids (remission). 2. Evaluate whether 1H high-resolution metabolic profiling of serum from patients with GCA/PMR associate with response to treatment and 3. Identify potential discriminatory serum metabolite profiles correlating with disease activity.

**Methods:** One-hundred and ten serum samples from 50 consecutive patients (33-GCA and 17-PMR) were evaluated in the study. GCA serum samples consisted of 33 naive, 22 in 1 and 21 after 6 months of treatment (25 females, mean age 73.0 ± 7.6 years and 8 males, mean age 69.5 ± 4.9 years), while PMR of 15 naive, 10 in 1st and 8 respectively (9 females, mean age 65.0 ± 5.3 years and 8 males, mean age 77.0 ± 6.6 years). The serum metabolic profiles of patients were obtained at a 600 MHz NMR spectrometer and analysed by means of univariate and multivariate statistical methods.

**Results:** Multivariate analysis showed metabolic differences between GCA/PMR patients in activity and in remission using unsupervised principal component analysis (PCA: R2X= 0.698, Q2= 0.561) and supervised partial least squares discriminant analysis (PLS-DA: R2X= 0.596, Q2= 0.219) (Figure 1). In accordance with univariate analysis (p<0.05), the following discriminatory metabolites were identified: N-acetyl glycoproteins, 3-hydroxybutyric acid and phenylalanine were increased in inflammation, while choline, lipoproteins, and lipids were decreased in these patients.

**Conclusion:** 1H NMR-based serum metabolomics revealed a clear discrimination of GCA/PMR metabolic profiles before (active inflammation) and after treatment with steroids (remission), suggesting that the metabolic analysis may serve as a useful tool to identify potential biomarkers related to disease activity in both GCA and PMR, as well as give further insights into pathogenetic mechanisms modulating the inflammatory response. Further validation studies to dissect the clinical value of specific metabolites are ongoing in our laboratory.

**REFERENCES:**
1. Robinette ML et al. Front Immunol 2021
2. Emwas A-M et al. Metabolites 2019

**Disclosure of Interests:** None declared.

**DOI:** 10.1136/annrheumdis-2022-eular.2646

---

**ARTERIAL WALL DENDRITIC CELLS IN GIANT CELL ARTERITIS (GCA) AND POLYMALGIA RHEUMATICA (PMR)**

A. Raman, H. Greigert, C. Cadière, M. Ciudad, P. Ornetti, B. Bonnotte, M. Samsoo, Dijon University Hospital, Rheumatology, Dijon, France; Bourgogne Franche-Comté University, INSERM, EFS BFC, UMR 1098, RIGHT Graft-Host-Tumor Interactions/Cellular and Genetic Engineering, Dijon, France; Dijon University Hospital, Internal Medicine and Clinical Immunology Department, Dijon-Bourgogne University Hospital, Dijon, France; Dijon University Hospital, Vascular Medicine Department, Dijon-Bourgogne University Hospital, Dijon, France

**Background:** Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disease (1) associated in 16 to 21% of cases with giant cell arteritis (GCA). The association of these two conditions raises the question of a pathophysiological continuum between PMR and GCA. An early study reported mature arterial wall dendritic cells (DC) in patients with GCA or PMR leading, during GCA, to CD4+ T cell recruitment and the development of vasculitis (2). However, these data have never been confirmed in other studies. There are 3 main types of DC: plasmacytoid DC (expressing CD123), conventional DC (cDC) expressing CD141 (cDC1) or CD1c (cDC2) and monocyte-derived DC (moDC) expressing CD14.

**Objectives:** The aim of this study was to describe the arterial wall infiltrating DCs, their phenotype and maturation state, during PMR and GCA.

**Methods:** Using temporal artery biopsies (TAB) from patients with PMR, GCA and healthy controls, the level of expression of CD11c, CD33, CCR7, CCR6, CD1c, CCL18, CCL19, CCL20, CCL21, GM-CSF, CD3, CD68 genes was assessed by RT-PCR. Expression of markers of DC lineage (CD209), DC maturation state (CD83 and CCR7) and DC origin (CD14, CD68, CD1c, CD141) were studied by confocal microscopy.

**Results:** Forty-one patients were included (14 GCA, 16 PMR, 11 controls). Within the arterial wall, DCs were identified in GCA patients, with a mature DC phenotype (CD209+/CD33+/CCR7+). DCs were present in all three layers of the arterial wall and also expressed CD14 and often CD68 but neither CD1c nor CD141, which could be explained by a monocytic/macrophage origin. TAB from GCA patients were characterized by a high level of expression of CD83, CCR7, CCR6, CCL18, CCL19, CCL20, CD11c, GM-CSF, CD3 and CD68 gene. This expression was significantly higher (p<0.05) compared to the control and PMR groups. Confocal microscopy analyses of arteries from the PMR and controls did not detect the presence of DCs into the arterial wall. In addition, level of