(RA).¹ Anti-CarP autoAbs target proteins that are modified through an irreversible post-translational modification named carbamylation.

Objectives The aim of this work was to assess whether anti-CarP antibodies can be used as a predictive factor of clinical response to abatacept.

Methods Peripheral blood samples of selected patients were collected at the beginning of the therapy with abatacept (T0) and every six months for one year (T6 and T12). A home-made ELISA was applied to determine serum anti-CarP levels. Commercial anti-citrullinated protein antibodies (anti-CCP3) (Inova Diagnostic), Rheumatoid Factor (RF) (Siemens) and high sensitivity C reactive protein (hsCRP) were also tested.

Results Sixty RA patients (49 female (81.2%)), all caucasian, treated with abatacept were enrolled. Fifty-three (88.3%) and fifty-six (93.3%) patients were also treated with corticosteroids and synthetic DMARD respectively. At baseline anti-CarP antibodies were found in 18 (30%) patients; RF and anti-CCP were positive in 35 (58%) and 51 (85%) patients respectively. Comparing anti-CarP+ with anti-CarP- patients at T0, anti-CarP+ group resulted younger ($p<0.01$) and with a longer disease duration ($p<0.05$); hsCRP was higher in anti-CarP+ group ($p<0.05$). Considering the entire cohort, a significant reduction of anti-CarP titre at T6 and T12 of treatment was shown ($p<0.0001$) while anti-CCP and RF titre did not show any significant change. Thirteen out of 18 patients anti-CarP+ were available for analysis at T6 and in 6 cases turned anti-CarP-. A significant reduction of DAS28-CRP at T6 was found in the subgroup of anti-CarP+ pts in comparison with the negative ones ($p=0.03$). No significant results were found dividing the cohort using the positivity to anti-CCP and/or RF. Furthermore, stratifying groups of patients for the combination of biomarkers, any groups including anti-CarP+ resulted in a trend towards a higher DAS28 reduction compared with the combination of anti-CCP+ and RF+ and anti-CAP- ones.

Conclusions The precocious onset and a longer disease duration in anti-CarP positive patients might suggest them as a specific risk factors for RA in this subgroup of patients. The link between the anti-CarP positivity at baseline and the higher reduction of disease activity during the first six months of treatment permitted us to hypothesize that anti-CarP antibodies, but not anti-CCP and/or RF, could be a predictive factor of a good clinical response to abatacept.

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Disclosure of Interest None declared.

P019 IS TREATMENT RESPONSE INFLUENCED BY BODY MASS INDEX IN JUVENILE IDIOPATHIC ARTHRITIS?

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Introduction There is evidence that obesity could be a risk factor for the severity and response to treatment in patients with RA due both to the mechanical effect of overweight and

to the potential pro-inflammatory effects of cytokines produced by adipose tissue.

Objectives To evaluate the role of overweight and obesity in a cohort of patients with Juvenile Idiopathic Arthritis (JIA), in terms of incidence, disease activity, outcome and response to treatments.

Methods This single-center retrospective cohort study evaluated 110 children affected by JIA under treatment with anti-rheumatic agents (DMARDs, biologic agents). Changes from baseline in ESR, CRP, number of active joints, and BMI were analyzed under each treatment until last visit. BMI categories of 5–84th (normal weight), 85–94th (overweight), and ≥ 95 th (obese) percentile were used. Patients with systemic JIA, uveitis, chronic comorbidities, or under other potentially confounding systemic treatments were excluded. Uni- and multivariate analyses were performed.

Results One hundred and ten JIA patients (polyarticular $n=50$, oligoarticular $n=38$, psoriatic $n=12$, enthesitis related arthritis $n=8$, undifferentiated $n=2$) were enrolled in the study, 75% girls, 25% boys. The mean age at treatment onset was 6.09 years. Baseline BMI was ≤ 84 th percentile in 80 patients, 85–94th in 27, and ≥ 95 th in 3.

We did not observe a significant association between BMI and ESR, CRP, or number of active joints at baseline, while involvement of the joints of lower limbs was significantly greater ($p=0.025$) in overweight/obese patients. We observed a trend toward lower remission rates and higher number of relapses, both after DMARDs and biologics, in patients with higher BMI.

Conclusions This study focuses on the relationship between overweight/obesity and JIA. A significant correlation between obesity and a greater involvement of the joints of the lower limbs was observed at baseline. Furthermore our data suggest that obesity could negatively influence the course of the disease as well as treatment response.

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P021 DIFFERENTIAL ACPA BINDING TO NUCLEAR ANTIGENS REVEALS A DISTINCT SUBSET OF ACETYLATION CROSS-REACTIVE AUTOANTIBODIES IN RHEUMATOID ARTHRITIS

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Career situation of first and presenting author Young investigator.

Introduction Anti-citrullinated protein autoantibodies (ACPA) in RA patients target a wide range of modified proteins and recent findings reveal that monoclonal ACPA are cross-reactive due to recognition of shared consensus citrulline-peptide motifs. Among physiological targets of ACPA, citrullination in neutrophil extracellular trap (NET) products, have been postulated to be important.

Objectives We sought to characterize the anti-nuclear and anti-neutrophil reactivities of different patient-derived monoclonal ACPA.

Methods The study included ten recombinant single B-cell derived RA monoclonal ACPA-IgG with CCP2 reactivity from different cell subsets and compartments (1, 2). They were screened for HEP-2 ANA reactivity, and binding to apoptotic cells or stimulated neutrophils. Binding was compared to CRISPR PAD4 KO cells and neutrophils from PAD2 and PAD4 KO mice. Immunoprecipitation and mass spectrometry were used to identify modified nuclear ACPA targets, and ELISA and Western blot for mAb binding to acetylated epitopes.

Results Four out of ten ACPA clones exhibited strong binding to apoptotic cells, nuclear binding to activated neutrophils, and reactivity to NETs. Three of these were ANA positive. Another NET-reactive ACPA instead displayed a cytoplasmic binding pattern. This cytoplasmic NET-binding was PAD4-dependent, whilst nuclear-mediated NET reactivity was PAD-independent. Using apoptotic cells, acetylated histones were confirmed to be the primary targets of the nuclear reactivity, which could be explained by consensus-motif driven ACPA cross-reactivity. Specifically targeted acetylated histone peptides were identified and the anti-modified protein autoantibody (AMPA) profiles of the ACPA were found to correlate with cell binding.

Conclusions When investigating monoclonal ACPA, our novel data reveal a distinct subset of ACPA with nuclear binding patterns and AMPA activity with acetylated histones (and not citrullinated proteins) in NETs and apoptotic cells.

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P022/O02 DISTINCT MACROPHAGE PHENOTYPE AND BIOENERGETIC PROFILES IN RHEUMATOID ARTHRITIS

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Introduction Synovial macrophages play a key role in RA disease progression, however, the diversity and plasticity of macrophage subsets and their metabolic profile within the joint has yet to be elucidated.

Objectives To phenotype distinct macrophage subsets within the RA joint, and determine the metabolic and inflammatory function of RA macrophages compared to healthy controls (HC).

Methods Synovial-tissue biopsies from RA, PsA and OA, obtained through arthroscopy, were digested to yield a synovial single cell-suspension. Biopsy suspensions and synovial fluid mononuclear cells were analysed using advanced flow-cytometry with the following antibody panel (CD40,CD45,CD64,CD68,CD163,CD206,CD253). CD14+ monocytes were sorted from RA and HC bloods and differentiated/polarized into M1/M2 macrophages. Inflammatory (IL-8,-MCP-1,-IL1b,-CCR5,-IRAK1,-OSM) and metabolic (HIF1a,-PFKFB3,-PKM2,-LDHA,-HK2) markers were measured by RT-PCR, and phagocytosis by OVA luciferase-yellow assays. Glycolysis (ECAR) and oxidative phosphorylation (OCR) were quantified by Seahorse -XFE- technology.

Results RA synovial-tissue and fluid CD68+ macrophages displayed markers typical of both M1(CD40+CD253+) and M2 (CD206+CD163+). A significant increase in frequency of CD68+ and CD64+ macrophages in synovial-tissue compared to fluid was observed (p<0.05), with significant increases in marker expression of CD40,CD163,CD206 (p<0.07). A spectrum of macrophage-subtypes within the inflamed joint was observed, with significant enrichment of a dominant double positive CD206+CD163+ macrophage subtype in the synovial-tissue versus synovial fluid demonstrated (p<0.05). Increased frequency of CD206+CD163+ macrophages and higher expression of activation marker CD40 were demonstrated in RA synovial-tissue compared to PsA and OA. M1 macrophages demonstrate a pro-glycolytic phenotype with significant increases in HIF1a,-HK2,-PKM2,-and PFKB3, compared to M2, effects exacerbated in RA macrophages compared to HC. In parallel, using seahorse-technology RA M1 and M2 macrophages displayed higher ECAR and OCR profiles, in addition to an increased ECAR:OCR ratio compared to HC (p<0.05), evidence that RA macrophages switch to a glycolytic profile. This was paralleled by increased intra-cellular-cytokines expression of IL-1b,-IL-6 and TNFα and genes expression of IL-8,-IL1b, OSM and MCP-1 (p<0.05). Finally, phagocytic ability of RA M1 was impaired compared to HC.

Conclusions We have identified, for the first time, a dominant macrophages subtype enriched in RA synovial-tissue. Furthermore, RA M1/M2 have distinct metabolic profiles associated with differences in key inflammatory mediator and phagocytosis function.

Disclosure of Interest None declared.

P023 TENOSYNOVITIS AND HLA-SE PREDICT ARTHRITIS ONSET IN ACPA-POSITIVE INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Career situation of first and presenting author Post-doctoral fellow

Introduction Anti-citrullinated protein antibodies (ACPA) are predictive markers with pathological effects in rheumatoid