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 homemade 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+ 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.

REFERENCE

Disclosure of Interest None declared.
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.

References

Disclosure of Interest None declared.

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

1AH Hensvold, 2Y Kisten, 3M Hanson, 4I Crönemar, 5M Sun, 6G Fei, 7E af Klint, 8H Rezaei, 9A Antovic, 10A Catrina. 1Inflammation and infection theme, Karolinska University Hospital. Rheumatology unit Karolinska Institutet; 2Centre for Rheumatology, Academic Specialist Center, Stockholm Health Services, Stockholm, Sweden

Career situation of first and presenting author Post-doctoral fellow

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