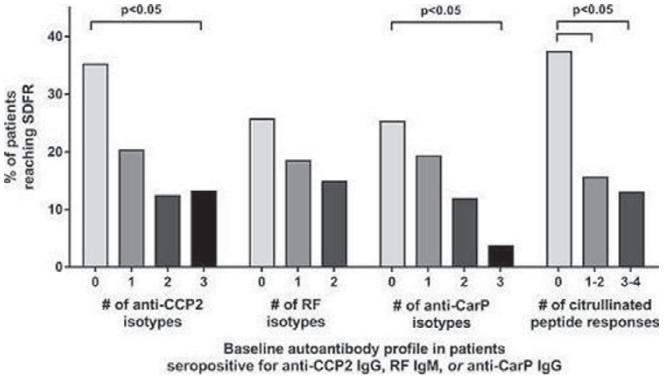
## AB0084 BREADTH OF BASELINE AUTOANTIBODY PROFILE AND TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

V.F.A.M. Derksen[1], E.C. de Moel[1], L.A. Trouw[1], R.J. Goekoop[2], I. Speyer[3], T.W.J. Huizinga[1], C.F. Allaart[1], R.E.M. Toes[1], D. van der Woude[1].
*[1]Rheumatology, Leiden University Medical Center, Leiden; [2]Rheumatology, Haga Hospital; [3]Rheumatology, Haaglanden Medical Center, The Hague, Netherlands*

**Background:** Seropositive and seronegative rheumatoid arthritis (RA) are distinct disease entities with regard to pathophysiological mechanisms and disease outcomes. However, over the past years it has become clear that the autoantibody profile of seropositive RA is very diverse, involving multiple post-translational modifications and isotypes, and it seems unlikely that a single autoantibody will be informative for identifying groups at risk of poor treatment response. Instead of individual autoantibodies, we hypothesized that the breadth of seropositive patients' profile may be the best reflection of the underlying immunopathology, and would be able to identify homogenous treatment response and inform treatment decisions.
**Objectives:** To investigate whether baseline autoantibody profile is associated with treatment response and the ability to taper off medication in RA patients.
**Methods:** All RA patients fulfilling the 2010 ACR/EULAR Criteria included in the IMPROVED study[1] that were seropositive for routine clinical testing for anti-cyclic citrullinated peptide-2 (anti-CCP2 IgG), rheumatoid factor (RF IgM), or our in-house assay for anti-carbamylated protein antibodies (anti-CarP IgG) were selected (n=381). In baseline sera of these patients, we measured IgG, IgM, and IgA isotypes for each family (except IgG for RF) and reactivity against 4 citrullinated peptides (cit-vimentin 59–74, cit-fibrinogen β 36–52 and α 27–43, and cit-enolase 5–20). We investigated associations between autoantibody profile and 1) change in disease activity score (DAS)-44 over time and 2) sustained drug-free remission, defined as the ability to taper off medication and remain in remission for ≥1 year after achieving DAS44<1.6.
**Results:** The initial treatment response (mean ΔDAS 0–4 months) in seropositive patients with a broad autoantibody profile (7–8 isotypes present) was better than in those with fewer isotypes present (ΔDAS 0–4 months of 7–8 isotypes vs 1–2, 3–4, and 5–6 isotypes, respectively: -2.2 vs -1.5 [p<0.001], -1.7 [p=0.04], and -1.8 [p=0.04]). In contrast, the presence of multiple autoantibodies was unfavorable regarding the long-term outcome of sustained drug-free remission. Within seropositive disease, patients with more isotypes and more reactivities to citrullinated peptides significantly less often achieved sustained drug-free remission (SDFR) (Figure).




**Conclusions:** Seropositive patients with a broader autoantibody profile at baseline initially react better to treatment, but are not able to taper off medication and remain in remission. This may be relevant in individualized decision-making for tapering medication, as these results suggest that disease with a broad autoantibody response, as proxy for an active humoral autoimmunity, is more difficult to control in the long-term without sustained therapy.
**References:**
[1] Heimans, AR&T 2016, 18:23.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2017-eular.3193

## AB0085 INTERACTION OF HLA-SHARED EPITOPE (SE) AND SMOKING ON THE DEVELOPMENT OF ANTI-CCP POSITIVE RHEUMATOID ARTHRITIS IN GREEK POPULATION

E.N. Mole[1], K. Tarassi[2], V. Kitsiou[2], T. Athanassiades[2], D. Kouniaki[2], K. Soufleros[2], C. Korkou[1], A. Tsirogianni[2], C. Sfontouris[1]. *[1]Department of Rheumatology; [2]Department of Immunology-Histocompatibility, Evangelismos General Hospital, Athens, Greece*

**Background:** Rheumatoid Arthritis (RA) is a complex, multifactorial autoimmune disease, whose etiopathogenesis involves genetic and environmental factors.
**Objectives:** The aim of the study was the assessment of the association of HLA-DRB1*-SE in the presence/absence of anti-CCP autoimmunity in Greek patients with RA (smokers and non-smokers).
**Methods:** Eighty-three (83) RA patients (41 smokers, 42 have never smoked) were typed for HLA-DRB1* alleles by molecular techniques (PCR-SSOP and -SSP). In 62 out of 83 (74.7%) anti-CCP abs were detected by ELISA.
**Results:** In RA pts and in comparison to the controls, increased frequency of HLA-DRB1*01:01 (28.9% *vs* 6.8%, OR=4.4), *10:01 (16.9% *vs* 2.4%, OR=8.4), *04:01 (3.6% *vs* 2%, OR=1.8), *04:04 (7.2% *vs* 1%, OR=7.6) and *04:05 (15.7% *vs* 3.7%, OR=4.8), as well as decreased frequency of *04:02 (1.2% *vs* 2%, OR=0.6) and *04:03 (4.8% *vs* 6.8%, OR=0.7) were found. Among the RA patients, 77.1% possess 1SE *vs* 18.9% of controls (OR=14.4), whereas 10.8% possess 2SE *vs* 1% of controls (OR=11.8). In CCP (+) RA patients and in comparison to CCP (-) an increased frequency of HLA-DRB1*01:01 (27.4% *vs* 14.3%, OR=2.3) and *10:01 (21% *vs* 4.8%, OR=5.3) was observed. Furthermore, 88.7% of CCP (+) carry 1SE *vs* 42.9% of CCP (-) patients (OR=10.5). CCP (+) smokers patients in comparison to CCP (+) non-smokers are presented with an increased frequency of DRB1*01:01 (41.9% *vs* 12.9%, OR=4.9). Among the CCP (+) smokers, 96.8% possess 1SE *vs* 80.6% of CCP (+) non-smokers (OR=7.2), whereas 12.9% possess 2SE *vs* 12.9% of CCP (+) non-smokers (OR=1).
**Conclusions:** a) An increased frequency of HLA-DRB1*01:01, *10:01, *04:05 alleles, as well as the protective role of *04:02, *04:03 alleles in Greek patients with RA were confirmed b) The presence of any SE, particularly *10:01 allele, strongly influences the production of anti-CCP abs and c) Interaction between smoking and any SE, particularly *01:01 allele, is associated with anti-CCP positive RA in Greek patients.
**References:**
[1] Klareskog L, Stolt P, Lundberg K, Kallberg H, Bengtsson C, Grunewald J, et al. A new model for an etiology of rheumatoid arthritis: smoking may trigger HLA-DR (shared epitope)-restricted immune reactions to autoantigens modified by citrullination. Arthritis and rheumatism. 2006;54(1):38–46.
[2] Ioannidis JP, Tarassi K, Papadopoulos IA, Voulgari PV, Boki KA, Papasteriades CA, et al. Shared epitopes and rheumatoid arthritis: disease associations in Greece and meta-analysis of Mediterranean European populations. Seminars in arthritis and rheumatism. 2002;31(6):361–70.
[3] Lee YH, Bae SC, Song GG. Gene-environmental interaction between smoking and shared epitope on the development of anti-cyclic citrullinated peptide antibodies in rheumatoid arthritis: a meta-analysis. International journal of rheumatic diseases. 2014;17(5):528–35.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2017-eular.5213

## AB0086 PREVENTIVE EFFECTS OF ANGIOTENSIN 1-7 ON NEOANGIOGENESIS AND LEUKOCYTE TRAFFICKING INCREASE IN THE EARLY PHASES OF AN EXPERIMENTAL MODEL OF ANTIGEN INDUCED ARTHRITIS

F. Fischetti, P. Durigutto, D. De Nardo, R. Carretta. *University of Trieste Italy, Trieste, Italy*

**Background:** Renin Angiotensin System (RAS) might be supposed to be involved in the early and late phases of development of synovitis, since data exist showing that Angiotensin (AT)-II contributes to the development of vascular damage under early inflammatory conditions (1, 2). Little is known about AT 1–7 functions, which is supposed to play counteracting actions vs AT II, under these conditions (2, 3)
**Objectives:** to evaluate if, in the early phases of an experimental model of arthritis, namely the antigen-induced arthritis (AIA), treatment with AT 1–7 could interfere with the synovial development of capillary vascular growth, and prevent leukocyte trafficking activation, in vivo, either at synovial and at mesentery post-capillary venules.
**Methods:** in compliance with European (86/609/EEC) and the Italian (D.L.116/92) ethics committees, 2 groups each of 8 male (240–270 gr) Wistar rats were randomly chosen and treated respectively with sterile saline, or with AT 1–7 (576 μg/kg/day), during the time of immunization with methylated serum bovine albumin (mBSA). Arthritis was induced by intraarticular administration of mBSA (0.1mg in 100ml sterile saline) into the right knee of each animal, after previous immunization to mBSA emulsified in complete Freund's adjuvant. The left knee, injected with only saline, served as a control. Two and 5 days after arthritis induction, the count of capillary branches, and the number of fluorescently-labelled leukocytes, showing transient or stable adhesion to the endothelial microvascular layer (EL), were assessed by using an in vivo videomicroscopy technique.
**Results:** synovial branching vessels with diameter >20μm were not modified after AIA induction, while microvessels having diameter less than 20 μm were significantly increased. After 2 and 5 days, AT 1–7 reduced the number of neo expressed <20μm diameter vessels (Day2: 3.7±3.4 vs 7.7±5.05, p=ns; Day5: 12.7±6.9 vs 21.0±7.3, p<0.05; both significantly greater than control joints). Transient and stable adhesion to EL showed to be partially reduced 2 days after AIA induction and significantly reduced after 5 days (Day5, transient=12.5±6.2 vs 26.0±9.0, p<0.05; stable=27.0±8.3 vs 41.7±10.6, p<0.05; both significantly greater than control joints). Comparable results were found when analysing the number of leukocytes adhering to mesentery EL.
**Conclusions:** we suggest that AT 1–7 could play an immune modulating role in the early phase of synovitis with possible prevention of further inflammatory and secondary structural tissue alterations. These data further support the hypothesis that mechanisms leading to synovial AT-II activation have a detrimental role in the development of arthritis.