polarization have been recognized: the ‘classically activated’ (M1) and the ‘alternatively activated’ (M2). miRNAs are a recently discovered class of post-transcriptional regulators. Of particular relevance in RA is miR155. Its expression is upregulated in RA synovial monocytes, macrophages and fibroblasts. Its overexpression in macrophages is associated to the production of pro-inflammatory mediators.

Objectives Here, we assessed monocytes capacity of differentiation into M2 and implication of miR155 in RA patients or controls (HD, CTD or SpA).

Methods Purified monocytes were incubated 6 day in the presence human serum AB (SAB) (M2). Expressions of total macrophages markers (CD11b-CD71), M2 markers (CD163, CD206, IL-10 and Arginase) and M1 markers (INOS, IFR5 and IL1 β) were evaluated by flow cytometry, ELISA or immunofluorescence. The microRNA transfections were performed using AMAXA technology.

Results We observed a significant decrease of macrophages induction only by SAB in RA patients as shown by a decreased expression of CD11b-CD71. We have found a specific decreased level of M2 markers. Moreover, we found *ex vivo* and *in vitro* that Adalimumab but not Etanercept or non-anti-TNF drugs were able to partially correct this defect of M2

We confirmed that under SAB treatment, RA monocytes have a propensity for preferential maturation towards a pro-inflammatory M1-like phenotype instead of M2, thus contributing to synovial inflammation.

We have hypothesized the involvement of miR155 on this defect. Indeed, miR155 is induced in monocyte or macrophages and drives their inflammatory response by epigenetic regulation that lead to M1 polarization. miR155 is increased in monocytes and M2 RA compared to controls.

Subsequently we transfected monocytes from HD with miR155 mimic and we observed a decrease differentiation in M2. Conversely preliminary experiments on RA monocytes transfection with a miR-155 inhibitor allowed the restoration of M2 polarization.

Conclusions RA patients have a specific impaired maturation of monocytes to M2 as much in phenotype and in function while the differentiation to the M1 phenotype is maintained. The use of monoclonal anti-TNF restores M2 polarization defect while Etanercept or non anti-TNF drugs do not restore M2.

This lack of M2 polarization is associated with miR155 increase in RA patients that leads to IFR5/INOS expression. Preliminary experiments showed that transfection of RA monocytes with an antagomiR155 may correct this lack of M2, justifying the proof of concept trial of monocytes-targeted nanoparticles containing microRNA in CIA mouse models.

Disclosure of Interest None declared.

P035

OCCUPATIONAL PHYSICAL WORKLOAD AND DEVELOPMENT OF ANTI-COLLAGEN TYPE II ANTIBODIES IN RHEUMATOID ARTHRITIS: RESULTS FROM THE SWEDISH EIRA POPULATION-BASED CASE-CONTROL STUDY

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Career situation of first and presenting author Young investigator.

Introduction Separate studies have previously observed an association between exposure to physical workload (PW) and risk of developing rheumatoid arthritis (RA). Levels of antibodies against collagen type II (CII), which are associated with HLA-DRB*01 and *03 are transiently elevated at the time of RA diagnosis. PW might impose mechanical stress on the articular cartilage where CII is the main constituent, leading to immune activation and production of anti-CII antibodies.

Objectives We hypothesize that exposure to PW would associate more strongly with anti-CII positive RA than with anti-CII negative RA.

Methods Data involving 2916 incident RA cases and 5130 controls from the Swedish Epidemiological Investigations in Rheumatoid Arthritis (EIRA) population-based case-control study were analysed. Information on exposure to PW was collected through questionnaires. The odds ratios (OR) with 95% CI of developing anti-CII positive RA or anti-CII negative RA was calculated using logistic regression.

Results The OR observed for the association between different types of PW and anti-CII positive RA ranged from 1.2 (0.8–1.8) to 1.7 (1.5–3.1). The OR for the association between PW and anti-CII negative RA ranged from 1.3 (1.1–1.4) to 1.6 (1.4–1.8). No statistically significant difference was observed between the OR for anti-CII positive RA and anti-CII negative RA (all p-values>0.10). Moreover, stratification for HLA-DRB*01 and *03 did not yield any statistical differences.

Conclusions We found no evidence suggesting an association between PW and elevated anti-CII levels at the time of diagnosis.

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Disclosure of Interest None declared.

P036

B CELL NUMBER REDUCTION HAS A PREDICTIVE VALUE FOR RESPONSE TO BELIMUMAB IN A COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Career situation of first and presenting author Student for a master or a PhD.

Introduction Belimumab, the anti-B-cell activation factor (BAFF) agent, is approved for the treatment of refractory systemic lupus erythematosus (SLE). Its effect on the number of circulating B-cells is selective on naïve (CD19+CD27-IgD+) and immature transitional B-cells (CD19+38high24high) whose survival is strictly BAFF-dependent. On the opposite, CD27+ memory B-cells are preserved during belimumab therapy, being their maturation more related to the activation of B-cell receptor pathways.

Objectives The aim of this study is the evaluation of B-cell subpopulations in a cohort of SLE patients treated with belimumab.

Methods Phenotypic analysis of peripheral blood B-lymphocytes was made by flow-cytometry in a cohort of SLE patients treated with belimumab. SLE-disease activity was assessed by SLEDAI-2K score. BAFF was tested by ELISA. SPSS was used for statistical analysis.

Results The relative change of BAFF levels at 6 and 12 months from baseline showed linear correlation with the percentage of naïve B-cells (Pearson correlation=0.645, $p=0.044$ and 0.639, $p=0.002$, respectively) and of transitional B-cells (Pearson correlation=0.768, $p=0.009$ and 0.623, $p=0.055$, respectively). The percentage and absolute number of naïve B-cells showed a progressive decrease during time (ANOVA, $p=0.013$ and $p=0.001$ respectively). In terms of response prediction, a significant association of SLEDAI percentage improvement at 12 months with the decrease of total number of B-cells within the first 6 months of therapy was observed (Log regression $r=0.707$, $p=0.05$).

Conclusions BAFF inhibition induces B-cell number modifications in a SLE cohort. The reduction of total number of B-cells within the first six months shows predictive value for SLEDAI response after the first year of therapy.

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Disclosure of Interest None declared.

P037

ANTI-CARBAMYLATED PROTEIN ANTIBODIES : ARE THEY USEFUL FOR THE DIAGNOSIS OF RHEUMATOID ARTHRITIS?

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Career situation of first and presenting author Resident.

Introduction The current EULAR-2010 diagnostic criteria for Rheumatoid Arthritis (RA) relies heavily on the presence of auto-antibodies. So far only anti-citrullinated peptide antibody (ACPA) or rheumatoid factor (RF) are accounted for however, novel auto-reactivities have been described notably anti-carbamylated protein (anti-CarP) and anti-oxylized peptide antibodies.

Objectives To investigate the potential of anti-CarP antibodies for the diagnosis of RA.

Methods 402 patients were recruited from an early arthritis register (ethically approved) with a diagnosis recorded over 24 months. 95 healthy controls were included. All participants provided written informed consent. An anti-CarP antibody ELISA was performed using carbamylated FCS as target antigen.¹ Results were expressed as aU/mL. Statistical analysis used ROC and AUC analysis established using SPSS V22.

Results We first determined the 95% CI of the distribution of ELISA results in HCs to define a negative/positive cut-off for the test, established at >250 aU/mL.

195/402 patient were classified as RA at inclusion; 28 developed RA over time while 56 remained undifferentiated arthritis; 83 had non persistent symptoms and 40 other inflammatory joint diseases.

Anti-CarP ELISA results were clearly much higher in RA (median 250 [IQR 25–762], $p<0.0001$) with 49% of patients being positive as well as in the group that progressed to RA (25% positive, 82 [13–235], $p=0.001$), compared to all other EAC patients together (8% positive, 26 [5–80]) or HC (5% positive, 41 [1–106]).

In this particular cohort, anti-CarP had an odd ratio OR=5.55 for predicting RA with a sensitivity SEN=91.5% and positive predictive value PPV=87%, compared to ACPA which had an OR=8.78 (SPE=92%, PPV=92%) and RF with an OR=4.18 (SPE=85%, PPV 84%).

Titres were not associated with other variables (age, gender, JC, CRP or DAS). A ROC analysis determined that linear data (aU/mL) for anti-CarP were not better than a positive/negative status at predicting RA.

A score counting the number of auto-antibodies (0–1–2–3) had a high predictive value (AUC=0.840, $p<0.0001$ SEN/SPE of 65%/95% and PPV/NPV of 94%/68%).

We then established that a combination of ACPA+antiCarP was superior at predicting RA (OR=25.1 SEN/SPE=43%/98.5%, PPV/NPV=97%/58%) than the ACPA+RF combination (OR=11.9, SEN/SPE=54%/95%, PPV/NPV=94%/62%), although less sensitive.

Conclusions Although RF is more frequently observed than anti-CarP, it is also less specific for RA. A combination of ACPA+anti CarP may prove more useful at classifying early arthritis patients for RA than an ACPA+RF combination. Future work needs to establish a standardised assay for anti-CarP and replicate this data.

Disclosure of Interest None declared.

P038

IN VIVO DEMONSTRATION OF TMTNF REVERSE SIGNALING: SIGNIFICANCE IN THE THERAPEUTIC RESPONSE TO ANTI-TNF AGENTS DURING MURINE ARTHRITIS

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Career situation of first and presenting author Post-doctoral fellow.

Introduction Anti-TNF agents are widely used in rheumatoid arthritis (RA). Their effect on inflammation results from the neutralization of soluble TNF (sTNF), but also supposedly from the induction of reverse signaling through their binding to membrane TNF (tmTNF). Despite possible clinical relevance, reverse signaling has been described only *in vitro* but has not been proven *in vivo*.

Objectives In this study we aim to demonstrate for the first time the existence of tmTNF reverse signaling *in vivo* and its importance in anti-TNF response during arthritis.

Methods Triple transgenic mouse model (3TG), KO for TNFR1/TNFR2 and KI for tmTNF, thus secreting no sTNF was developed. To analyze reverse signaling, mice were injected