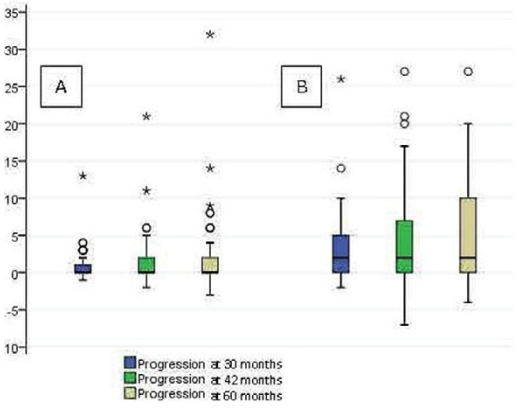
14–3-3η since HIGH 14–3-3η were then present in 32/162 (19.7%) SJC=0 patients; 22/108 (20.4%) SJC+TJC=0 and 13/56 (23.2%) Boolean.
Compared to patients in remission with LOW 14–3-3η, patients in remission with HIGH 14–3-3η at 18 months had numerically faster subsequent progression with all definitions. For example, in patients with Boolean remission, mean (SD) erosion progression over 42 months was 7.2±13.1 vs 1.5±3.3 and mean (SD) progression of Total score 9.2±14.5 vs 2.8±4.4 units (Figure).
However, due to low numbers and limited power, differences in progression were statistically significant only for the less strict definitions of remission and only over the following year: Erosions (SJC=0, p=0.0042, SJC+TJC=0, p=0.0236), Total score (SJC=0, p=0.0146; with a trend for SJC+TJC=0, p=0.077).
None of the comparisons over 42 months or of those involving Boolean reached significance.

Figure. Progression of Erosion Sharp/van der Heijde score in patients in Boolean remission at 18 months.
A. 14-3-3η <0.50 ng/ml at 18 months. **B.**14-3-3η ≥0.50 ng/ml at 18 months.



Conclusions: The persistence of 14–3-3η levels ≥0.50 ng/ml appears to be associated with a lower probability of reaching remission in polyarthritis patients. 14–3-3η levels ≥0.50 ng/ml in patients in clinical remission appear to be associated with more rapid radiographic (especially erosive) progression over the following year. A larger study is required to validate these findings, especially with the most stringent criterion of Boolean remission.
Disclosure of Interest: N. Carrier: None declared, M.-P. Garant: None declared, A. Marotta Employee of: Augurex Life Sciences Corp., A. De Brum Fernandes Grant/research support from: AJdBF is part of the Centre de Recherche Clinique from the CHUS, which received a team grant from the Fonds de Recherche en Santé-Québec, P. Liang: None declared, A. Masetto: None declared, Y. Gui Employee of: Augurex Life Sciences Corp., J. Savill Employee of: Augurex Life Sciences Corp., S. Michienzi Employee of: Augurex Life Sciences Corp., W. Maksymowych Consultant for: Augurex Life Sciences Corp., G. Boire Grant/research support from: GB is part of the Centre de Recherche Clinique from the CHUS, which received a team grant from the FRSQ. GB is the recipient of CIHR grant MOP-110959. Since 2007, the Sherbrooke EUPA cohort has also received financial support from the Canadian ArTritis CoHort (CATCH), a study designed and implemented by investigators and financially supported via unrestricted research grants initially by Amgen Canada Inc
DOI: 10.1136/annrheumdis-2017-eular.4085

FRI0048 THE ANTI-CD20 ANTIBODY RITUXIMAB REDUCES THE INFLAMMATORY AND PROTHROMBOTIC PROFILE OF LEUKOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS AND MODULATES THE ACTIVITY OF ENDOTHELIAL CELLS

I. Cecchi[1], C. Perez-Sanchez[2], P. Ruiz-Limon[2], I. Arias de la Rosa[2], M.C. Abalos-Aguilera[2], Y. Jimenez-Gomez[2], R. Ortega[2], E. Collantes-Estevez[2], A. Escudero[2], N. Barbarroja[2], S. Sciascia[1], C. Lopez-Pedrera[2]. *[1]Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases - Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Turin, Italy; [2]GC-5/Rheumatology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain*

Background: Rituximab (RTX) has been shown to be successful in the treatment of rheumatoid arthritis (RA), indicating that B cells have an important role in this disease.
Objectives: The present study was undertaken to investigate the mechanisms of action of RTX on the immune and endothelial cells (EC) of the vascular system in the setting of RA.
Methods: Purified lymphocytes from five RA patients with high disease activity were treated with RTX (1ug/mL) for 24 hours. Then, the depletion of B cells was assessed by flow cytometry, and the changes occurred in the inflammatory profile of T-lymphocytes was analysed by RT-PCR. In a second set of experiments, to evaluate the influence of B-cell depletion on the inflammatory/prothrombotic profile of cells belonging to the vascular system, supernatants from cultured lymphocytes of RA patients in the presence or in the absence of RTX were added to isolated monocytes from AR patients and to cultured endothelial cells. The response to RTX was then examined.
Results: As expected, RTX promoted a significant depletion of B-cells. In parallel, the inflammatory profile of T lymphocytes from RA patients was downregulated, as shown by a significant drop of IL-1, IL-6, IL-17, IFN and TNF expression levels, thus suggesting that the anti-inflammatory effects of RTX might be related to B cell depletion. Supernatants from RTX-treated lymphocytes further abridged the prothrombotic profile of RA-monocytes, promoting a significant inhibition of TF, MCP-1, IL-8, IL-1 and VEGF-A gene expression. Moreover, endothelial cells, activated after treatment with supernatants from cultured RA-lymphocytes, showed reduced expression of cell-adhesion molecules (i.e. V-CAM, I-CAM, E-Selectin) and pro-thrombotic factors (i.e. TF, VEGF, IL-8) after treatment with supernatants from cultured RA-lymphocytes in the presence of RTX.
Conclusions: Overall, these results reveal that depletion of B-cells by RTX in RA influences the inflammatory profile of T lymphocytes, as well as their interaction with monocytes and ECs, thus modulating the inflammatory and prothrombotic shape of vascular cells in the setting of RA.
Acknowledgements: Supported by CTS-794, ISCIII (PI15/01333; RIER RD16/0012/0015)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4916

FRI0049 FC GAMMA RECEPTOR IV ENHANCES BONE EROSION IN EXPERIMENTAL ARTHRITIS BY PROMOTING INFLUX OF PMNS

I. Di Ceglie[1], G. Ascone[1], M. van den Bosch[1], J.S. Verbeek[2], P. van der Kraan[1], P. van Lent[1]. *[1]Experimental Rheumatology, Radboud University Medical Center, Nijmegen; [2]Leiden University Medical Center, Leiden, Netherlands*

Background: FcγRs are involved in regulation of synovial activation and bone destruction during immune complex (IC)-mediated arthritis. The balance between activating FcγRs (FcγRI,III and IV) and inhibiting FcγRII determines synovial activation. Here we investigated the particular role of activating FcγRIV in bone erosion in IC-mediated antigen induced arthritis (AIA) by comparing FcγRI,II,III,IV$^{-/-}$ mice, FcγRI,II,III$^{-/-}$ mice and wild type controls (WT).
Objectives: To investigate the role of FcγRIV in bone erosion during experimental arthritis.
Methods: AIA was induced by injection of mBSA into knee joints of mice previously immunized with mBSA/CFA. Joint inflammation, bone destruction, number of TRAP^{+} osteoclasts and S100A8/A9 positive cells was determined using histology and immunohistochemistry. *In vitro* osteoclastogenesis was assessed using TRAP staining.
Results: Seven days after induction of AIA, we observed decreased inflammation and bone erosion in the knee joints of FcγRI,II,III,IV$^{-/-}$ mice compared to WT. The ability of bone marrow cells of FcγRI,II,III,IV$^{-/-}$ mice to differentiate into osteoclasts *in vitro* was comparable to the one of WT controls. Moreover, we observed comparable numbers of TRAP^{+} osteoclasts on the bone surface of FcγRI/II/III/IV$^{-/-}$ and WT arthritic mice, suggesting that the observed decrease in bone erosion is mainly caused by a reduced osteoclast activity, rather than decreased osteoclast number. However, in contrast to FcγRI/II/III/IV$^{-/-}$, AIA induction in knee joints of FcγRI/II/III $^{-/-}$ resulted in increased bone erosion and inflammation compared to WT, highlighting the possible crucial role of FcγRIV in the pathology. Interestingly, the number of PMNs infiltrated in the knee joint of FcγRI/II/III$^{-/-}$ resulted increased, whereas it was decreased in the knee joints of FcγRI/II/III/IV$^{-/-}$ compared to their WT controls. This observation suggests that particularly FcγRIV is involved in regulating influx of PMNs. PMNs are potent producers of alarmins S100A8/A9 which are described to promote osteoclast activity. In line the number of S100A8/A9 positive cells in synovium was increased in FcγRI/II/III$^{-/-}$ while decreased in FcγRI/II/III/IV$^{-/-}$, compared to their WT control.
Conclusions: FcγRIV promotes bone erosion in AIA by enhancing influx of PMNs within the synovium. PMNs are potent producers of S100A8/A9 which has been described to induce osteoclast activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5386

FRI0050 TYPE II COLLAGEN SECRETED FROM ARTICULAR CHONDROCYTES IS MAINLY DESTROYED BY CATHEPSIN S IN RA MICE

J. Zhao, Q. Huang, H. Ren, M. Yang. *Department of Rheumatology, Nanfang Hospital, Southern Medical University, Guangzhou, China*

Background: Mast cells have long been recognized to increase strikingly in number in the synovial membrane of rheumatoid arthritis (RA), accounting for 5% of the surface synovial membrane cells. Type II collagen has the longest half-life in cartilage matrix. The main cells which might affect articular cartilage in RA are synovial fibroblasts, synovial macrophages and mast cells. The latter two could express cathepsin S.
Objectives: We aimed to find the cells which have the biggest influence on type II collagen secreted from articular chondrocytes and the possible mechanisms in RA mice.
Methods: Four types of cells from collagen-induced arthritis model-established C57BL/6 mice were primary cultured, including synovial fibroblasts, peritoneal

macrophages, bone marrow-derived mast cells and articular chondrocytes. The first three were co-cultured with articular chondrocytes separately. LHVS, a specific inhibitor of cathepsin S, and E64, a broad-spectrum inhibitor of cysteine protease, were added into the cocultures of macrophages and articular chondrocytes separately. Also, C48/80, an activator of mast cells, LHVS, and E64 were added into the cocultures of mast cells and articular chondrocytes separately. The culture supernatant fluid was collected. The concentration of cathepsin S and type II collagen were measured by ELISA. The expression of type II collagen mRNA in each group was detected with RTPCR.

Results: Macrophages and mast cells expressed cathepsin S, while synovial fibroblasts did not express cathepsin S. Synovial fibroblasts had little effect on the expression of type II collagen from articular chondrocytes. When articular chondrocytes were co-cultured with macrophages, the expression of type II collagen decreased (8.79±2.79ng/ml),compared with the control group (17.75±7.84ng/ml). The secretion of type II collagen could return to normal by the inhibitors of cathepsin S, both LHVS (16.15±8.05 ng/ml) and E64 (12.55±6.64 ng/ml). When articular chondrocytes were co-cultured with mast cells, the type II collagen could be restrained by C48/80 (9.82±0.42ng/ml), compared with the control group (26.09±9.34ng/ml). Similarly, the secretion of type II collagen could return to normal by LHVS and E64 (16.15±8.05 ng/ml, 12.55±6.64 ng/ml, respectively). There was no significant difference in the expression of type II collagen mRNA between different groups. It showed that the type II collagen was not suppressed at the transcription level, but was mainly destroyed by cathepsin S after secretion.

Conclusions: Macrophages and mast cells are the major sources of cathepsin S, which might be the main factor that destroys type II collagen secreted from articular chondrocytes in RA mice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5664

FRI0051 EARLY ARTHRITIS INDUCES DISTURBANCES AT BONE NANOSTRUCTURAL LEVEL REFLECTED IN DECREASED TISSUE HARDNESS

B. Vidal[1], R. Cascão[1], M. Finnilä[2,3], I. Lopes[1], S. Saarakkala[2,4,5], P. Zioupos[6], H. Canhão[7], J. Fonseca[1,8]. *[1]Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal; [2]Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, Oulo; [3]Department of Applied Physics, University of Eastern Finland, Kuopio; [4]Medical Research Center Oulo, Oulu University; [5]Department of Diagnostic Radiology, Oulu University Hospital, Oulo, Finland; [6]Biomechanics Labs, Cranfield Forensic Institute, Cranfield University, Swindon, United Kingdom; [7]EpiDoC Unit, CEDOC, NOVA Medical School, NOVA University; [8]Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon Academic Medical Centre, Lisboa, Portugal*

Background: Arthritis induces joint erosions and skeletal bone fragility.

Objectives: The main goal of this work was to analyze the early arthritis induced events at bone tissue level.

Methods: Eighty-eight Wistar rats were randomly housed in experimental groups, as follows: adjuvant induced arthritis (N=47) and a control healthy group (N=41). Rats were monitored during 22 days for the inflammatory score, ankle perimeter and body weight and sacrificed at different time points (11 and 22 days post disease induction). Bone samples were collected for histology, micro-CT, 3-point bending, nanoindentation and Fourier transformed infrared spectroscopy (FTIR) analysis. Blood samples were also collected for bone turnover markers and systemic cytokine quantification.

Results: At bone tissue level, measured by FTIR analysis and nanoindentation, there was a reduction of the mineral and collagen content and of hardness in the arthritic group, associated with an increase of the ratio of bone concentric to parallel lamellae and of the area of the osteocyte lacuna. In addition, increased bone turnover and changes in the microstructure and mechanical properties were observed in arthritic animals, since the early phase of arthritis, when compared with healthy controls.

Conclusions: Arthritis induces very early changes at bone tissue level characterized by decreased tissue hardness and of collagen and mineral content. These observations highlight the pertinence of immediate control of inflammation in the initial stages of arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3509

FRI0052 SALIVARY PEPTIDYL-ARGININE DEIMINASE AND TANNERELLA FORSYTHIA ARE ASSOCIATED WITH CLINICAL ACTIVITY OF RHEUMATOID ARTHRITIS

D.-X. Xibillé-Friedmann[1], J.-I. Martínez-Rivera[2], M.-A. De la Garza-Ramos[3], J. González-Christen[4], S.-M. Carrillo-Vázquez[5], J.-L. Montiel-Hernandez[4]. *[1]SEIC, Servicios de Salud de Morelos; [2]CISEI, Instituto Nacional de Salud Pública, Cuernavaca; [3]CIDICS/Facultad de Odontología, Universidad Autonoma de Nuevo Leon, Monterrey; [4]Facultad de Farmacia, Universidad Autonoma del Estado de Morelos, Cuernavaca; [5]Hospital Regional 1o. Octubre, ISSSTE, Mexico city, Mexico*

Background: Although the expression of bacterial Peptidyl-Arginine Deiminase (PAD) derived from *P. gingivalis* seems critical in explaining the potential effects of severe periodontitis in the development of Rheumatoid arthritis (RA), the association with the presence of the bacteria or anti-P. gingivalis/anti-PPAD antibodies is not always evident suggesting that other bacteria could be involved in the link between oral microbiota and citrullination of host proteins.

Objectives: To confirm the association between RA disease activity in a homogeneous population (aCCP+ RA patients), oral PAD activity and the prevalence of other bacterial strains such as *T. forsythia*.

Methods: RA patients fulfilling ACR/EULAR 2010 criteria were evaluated from a periodontal (Periodontal Screening Recoding Index) and rheumatologic standpoint. Patients with Sjögren's syndrome or sicca symptons were excluded. Disease activity was measured using DAS28 (ESR). Oral PAD activity was measured by colorimetric assay and presence of *Porphyromonas gingivalis, Tannerella forsythia* and *Prevotella intermedia* was evaluated by PCR. Autoantibody levels were determined by ELISA. Multivariate analysis adjusted for gender, age, time since onset of disease, RF and ESR. Comparisons between groups were performed by Mann-Whitney U testing or Kruskal–Wallis testing per the t variables. Spearman correlation testing was employed to correlate PAD activity and DAS28. Statistical significance was set at 0.05%.

Results: 132 patients were included. After a multivariate analysis an association was observed between severe periodontitis/dental mobility with moderate/high RA disease activity (OR: 4.4 (1.8–14.0), p=0.04 and 3.4 (1.1–13.4), p=0.03, respectively). Additionally, presence of *P. gingivalis* and *T. forsythia*, but not *P. intermedia*, was significantly associated with moderate/high RA disease activity (3.4 (1.1–10.5), $p<0.05$ and 4.4 (1.2–10.9), $p<0.05$). Comparing PAD activity in saliva samples of RA patients we found significant differences between the low (2.3±0.5), moderate (3.4±0.8) and high (4.3±0.3) disease activity subgroups ($p<0.01$%), whereas patients in remission demonstrated a PAD activity similar to the low disease activity group (1.9±0.39). Additionally, we found a significant correlation between oral PAD activity and RA activity, but not with autoantibody titers.

Conclusions: These results show that RA activity is associated with severe periodontitis, high oral PAD activity and the presence of *T. forsythia* and *P. gingivalis*, suggesting that both bacteria equally participate in PAD activity present in the oral microenvironment.

Acknowledgements: Disclosure: This work was supported by a grant from SEP/CONACYT CB-2010 (#155392).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3894

FRI0053 ANTIBODIES TO A SUBSET OF CITRULLINATED PEPTIDE ANTIGENS CORRELATE WITH NEUTROPHIL EXTRACELLULAR TRAP LEVELS IN THE SPUTUM OF SUBJECTS AT-RISK FOR FUTURE RA

K.D. Deane[1], M. Purmalek[2], N.L. Seto[2], E. Bowers[1], J.M. Norris[3], V.M. Holers[1], W. Robinson[4], M. Kaplan[2], M.K. Demoruelle[1]. *[1]Division of Rheumatology, University of Colorado Denver, Aurora; [2]Systemic Autoimmunity Branch, National Institutes of Health/NIAMS, Bethesda; [3]Epidemiology, Colorado School of Public Health, Aurora; [4]Division of Immunology and Rheumatology, Stanford University, Palo Alto, United States*

Background: Prior data suggest that anti-citrullinated protein/peptide antibodies (ACPA) may originate in the lung prior to the onset of synovitis in rheumatoid arthritis (RA) (1). Neutrophil extracellular trap (NET) formation is one potential mechanism that could trigger or be associated with local ACPA generation because NETs externalize citrullinated proteins and release peptidylarginine deiminase that could citrullinate nearby proteins (2–4).

Objectives: Using induced sputum, we recently identified a significant correlation between NETs and anti-cyclic citrullinated peptide (CCP) antibodies in subjects at-risk for future RA. Herein, we sought to explore associations of individual ACPAs and NETs in these subjects.

Methods: From the Studies of the Etiology of RA (SERA) cohort, we included 24 RA-free subjects At-Risk for future RA based on familial (i.e. first-degree relative of RA patient) or serologic (i.e. serum anti-CCP positive identified at health fairs) risk. Induced sputum was tested using a bead-based ACPA array for IgG reactivity to 29 individual citrullinated proteins/peptides. Levels of NET complexes in sputum were measured using a deoxyribonucleic acid (DNA)-myeloperoxidase (MPO) and DNA-neutrophil elastase (NE) sandwich ELISA. Analyses included Spearman's correlation and linear regression. Using Bonferonni's correction, results were considered significant if both DNA-MPO and DNA-NE assays had a $p<0.002$.

Results: Subjects had a median age of 51 years, were 67% female and 38% ever-smokers. Increasing sputum NET levels significantly correlated with increasing ACPA levels for 27/29 ACPAs, including proteins/peptides of cit-vimentin, cit-fibrinogen, cit-fibronectin, cit-apoliporoteins and cit-alpha-enolase. After adjusting for ever-smoking, sputum NET levels remained significantly associated with 17/29 ACPAs. The strongest associations ($p\leq0.001$ for both NET assays) were cit-H2A/a2$_{1–20}$, cit-vimentin$_{58–77\ \text{cyclic}}$, cit-alpha-enolase$_{5–21}$, cit-fibrinogen$_{27–43}$, cit-fibrinogen$_{211–230\ \text{cyclic}}$, cit-fibrinogen$_{616–635\ \text{cyclic}}$, cit-fibrinogenB$_{54–72}$, and cit-apolipoprotein E$_{277–269\ \text{cyclic}}$.

Conclusions: In subjects At-Risk for future RA, we identified a strong corre-