REFERENCE

1. Manivel VA, Mullazehi M, Padyukov L, *et al*. Anticollagen type II antibodies are associated with an acute onset rheumatoid arthritis phenotype and prognosticate lower degree of inflammation during 5 years follow-up. *Annals of the Rheumatic Diseases* 2017;**76**(9):1529–1536. doi:10.1136/annrheumdis-2016-210873

Acknowledgements The MyEIRA study group- Chiara Berretta, Heselynn Hussein, Wahinuddin Sulaiman, Ing Soo Lau, Suk Chyn Gun, Nor Suhaila Sharil, M. Eashwary, Mohamed Said Mohd-Shahrir, Ainon Mohd Mokhtar, Azmillah Rosman, Muhaini Othman, Lars Alfredson and Lars Klareskog.

Disclosure of interest None declared

P048 ABSTRACT WITHDRAWN

P049 CHARACTERISATION OF THE ANTIBODY RESPONSE TO A CITRULLINATED PEPTIDE DERIVED FROM PORPHYROMONAS GINGIVALIS PAD IN RA

[1]N Kharlamova*, [2]B Brynedal, [1]N Sherina, [3]K Eriksson, [3]T Lindberg, [1]M Hansson, [1]L Israelsson, [1]J Steen, [1]V Malmström, [2]L Alfredsson, [1]K Amara, [1]K Lundberg. *[1]Department of Medicine; [2]Environmental Medicine; [3]Dental Medicine, Karolinska Institutet, Stockholm, Sweden*

10.1136/annrheumdis-2018-EWRR2018.68

Introduction Anti-citrullinated protein antibodies (ACPA) – a hallmark of rheumatoid arthritis – antedate joint inflammation. Based on the epidemiological association between RA and periodontal disease (PD),[1] it has been suggested that break of tolerance to citrullinated proteins may occur in the gum mucosa. This hypothesis is primarily based on the unique feature of *Porphyromonas gingivalis* (*P.g*) – a keystone pathogen in PD – to express a bacterial version of the peptidyl arginine deiminase enzyme (denoted *P.*PAD), capable of autocitrullination.[2]

Objectives In the present study, we have investigated the antibody response against CPP3, a citrullinated peptide derived from *P.*PAD, in order to address the hypothesis that *P.g* may drive ACPA-production.

Methods

This study included 2,859 RA cases and 4864 controls from the Epidemiological Investigation of RA (EIRA) cohort; 65 PD patients and 59 periodontally healthy individuals; and 218 monoclonal antibodies, derived from RA B cells. Reactivity with citrullinated *P.g* and human antigens was assayed by ELISA and/or multiplex. Associations with genetic risk factors and smoking were determined by logistic regression. Monoclonal antibody mutations were analysed by IgBLAST comparison.

Results Anti-CPP3 IgG was detected in 11% of RA, 10% of PD and <2% of controls, with higher levels in RA compared to PD. These antibodies clustered outside the classical ACPA response, associated with smoking, but not with major genetic risk factors. Two CPP3-reactive monoclonal antibodies were identified; one which cross-reacted with citrullinated human vimentin and had extensive mutations, indicating antigen-driven clonal selection and affinity maturation.

Conclusions Based on these data, we propose that *P.g* infection triggers an antibody response to CPP3, which cross-reacts with citrullinated human proteins by mechanisms of molecular mimicry. Future studies should address whether anti-CPP3 IgG could serve as a biomarker to identify individuals with PD at increased risk for RA.

REFERENCES

1. Fuggle NR, Smith TO, *et al*. Hand to mouth: A systematic review and meta-analysis of the association between rheumatoid arthritis and periodontitis. *Frontiers in Immunology* 2016;**7**:80.
2. Quirke AM, *et al*. Heightened immune response to autocitrullinated porphyromonas gingivalis peptidylarginine deiminase: A potential mechanism for breaching immunologic tolerance in rheumatoid arthritis. *Annals of the Rheumatic Diseases* 2014;**73**(1):263–269.

Disclosure of interest None declared

P050 HIGH CHOLESTEROL LEVELS BY APOE DEFICIENCY REDUCE BONE DESTRUCTION IN ANTIGEN-INDUCED ARTHRITIS VIA REDUCTION OF THE NUMBER OF OSTEOCLASTS

[1]G Ascone, [1]I Di Ceglie, [1]M van den Bosch, [1]A Sloetjes, [1]P van der Kraan, [2]E Lindhout, [1]A Blom, [1]P van Lent*. *[1]Experimental Rheumatology, Radboud university medical centre, Nijmegen; [2]Future Diagnostics Solutions (FDx), Wijchen, Netherlands*

10.1136/annrheumdis-2018-EWRR2018.69

Introduction Rheumatoid arthritis (RA) is a chronic inflammatory disease characterised by immune complex (IC) deposition in the synovium, leading to increased bone destruction. In RA, joint destruction has been associated with high levels of low density lipoproteins (LDL) and enhanced LDL oxidation (oxLDL). Apolipoprotein E (Apoe) is an important regulator of LDL transportation and its absence strongly elevates circulating LDL levels, which may lead to increased oxLDL levels during inflammation.

Objectives In this study, we investigated the effects of high LDL levels on bone destruction during antigen-induced arthritis (AIA) and how increased LDL/oxLDL levels affect osteoclast formation.

Methods AIA was induced by injection of methylated BSA (mBSA) into the right knee joint of *Apoe*$^{-/-}$ and wild type (WT) control mice previously immunised with mBSA and complete Freund's adjuvant (CFA). WT and *Apoe*$^{-/-}$ Hoxb8 myeloid precursor cells were differentiated into osteoclasts using 20 ng/mL RANKL and 30 ng/mL M-CSF, then stimulated for 24 hour with 10 µg/mL LDL/oxLDL. Oil Red O staining was performed to assess lipid uptake by osteoclasts. mRNA levels of c-Fos, RANK, NFATc1, DC-STAMP, TRAP, CTR, ClC-7 and Cat K were measured by qPCR. Bone erosion was quantified by histological analysis using an arbitrary scale from 0 to 3 and TRAP^{+} cells were determined using immunohistochemistry.

Results *Apoe*$^{-/-}$ mice showed significantly higher LDL serum levels than WT controls. At day 21 after AIA induction, bone erosion was significantly decreased in *Apoe*$^{-/-}$ mice (25% reduction from 1.5±0.2 to 1.1±0.1). In line with that, the number of osteoclasts within the knee joints was 36% lower in *Apoe*$^{-/-}$ mice, as determined by image analysis of TRAP staining. To study the role of Apoe and high LDL levels on osteoclastogenesis in more detail, we differentiated WT and *Apoe*$^{-/-}$ myeloid precursor cells (Hoxb8) into osteoclasts and found similar mRNA levels of osteoclast markers. Whereas LDL stimulation did not affect osteoclast formation, oxLDL strongly impaired cell fusion keeping them in a mononuclear state. mRNA levels of DC-STAMP were significantly downregulated in both WT and *Apoe*$^{-/-}$ osteoclasts (1.4 and 2.3 fold decrease, respectively) as well as TRAP activity (49% and 58% reduction in WT and *Apoe*$^{-/-}$ osteoclasts), underlining a major role of oxLDL in inhibiting osteoclastogenesis.