with RA-associated *E. lenta* on alternate days for one week and were induced for arthritis. Gavage with microbes continued for 4 weeks. Mice were monitored for onset and progression of arthritis. Epithelial integrity was done by FITC-Dextran assay and citrulline levels in faecal and plasma samples were measured by liquid chromatography mass spectrometry

Results: Mice gavaged with *E. lenta* showed a much higher load of gut microbes compared to controls. Surprisingly, *E. lenta* did not augment gut permeability as it was similar to non-gavaged arthritic mice. *eggerthella lenta* is involved in ornithine pathway leading to generation of citrulline. To test if gavage with *E. lenta* accumulates citrulline in the gut, we tested citrulline levels in faecal samples by liquid chromatography mass spectrometry. Surprisingly, mice gavaged with *E. lenta* had lower levels of citrulline in faecal samples as compared to mice naïve mice with no gavage or arthritic mice without gavage. One can speculate from these observations that there is an expansion of commensals, like *E. lenta* in RA, leading to production of citrulline. To determine if citrulline could be accumulated outside of gut, we measured citrulline in sera of mice in various groups, gavaged with *E. lenta*, naïve and mice induced for arthritis but no *E. lenta* gavage. Surprisingly, mice gavaged with *E. lenta* and induced for arthritis had lower levels of citrulline as compared to controls induced for arthritis but no gavage, $p < 0.05$. Naïve mice gavaged with *E. lenta* also showed significantly much lower levels compared to sera of naïve mice.

Conclusions: This data suggests that *E. lenta* may be a major player in determining certain metabolic pathways. If Citrulline is being converted to arginine and used in other pathways is currently under investigation. Our studies suggest that gut commensals influence immune response in and away from the gut. Commensals and their products may provide novel targets for therapeutic strategies in arthritis.

REFERENCE:

- [1] Chen J, Wright K, Davis J, Marietta E, Luckey D, Jeraldo P, Murray J, Nelson H, Matteson E, Taneja V. An expansion of rare lineage intestinal microbes characterizes rheumatoid arthritis Genome Medicine 2016;8:43. doi:10.1186/s13073-016-0299-7

Acknowledgements: The US Department of Defense grant W81XWH 15-1-0213 and the Centre of Individualised Medicine, Mayo Clinic

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3179

AB0138 THE BONE MARROW OEDEMA IS LINKED TO A OSTEOCLASTIC ENVIRONMENT IN BONE MARROW DURING COLLAGEN INDUCED MICE ARTHRITIS DEVELOPMENT

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Background: Bone erosion is a central pathogenic event in Rheumatoid arthritis (RA) and is associated with joint damage and poor functional outcome. The synovitis is traditionally regarded as the primary event of bone erosion in RA and synovial cells are usually thought to play a critical role in this pathologic process. However, the synovitis-centred concept has long been challenged by recent clinical finds. Bone erosion formation also could be found in joints without clinical traits of synovitis, suggesting that synovitis and joint erosion could be uncoupled. Moreover, recent study demonstrated that bone marrow oedema (BME) that identified by magnetic resonance imaging (MRI) is strongly associated with erosive progression, which independent of local synovitis in RA.

Objectives: BME is also called osteitis, which represent the replacement of adipose tissue with inflammatory cells in bone marrow. In this study we addressed 2 questions: 1) the course of BME and synovitis in a same joint during CIA development; 2) how BME cause the bone erosion in CIA.

Methods: Using collagen induced mice arthritis model, we compared the compared the time course of appearance of BME, synovitis and arthritic symptoms during the development of CIA. The changes RANKL, cytokines, osteoclast and immune cells expression in bone marrow during the development of CIA were analysed by flow cytometric analysis, immunofluorescence staining and RT-qPCR.

Results: MRI BME can be identified as early as 25 days after first immunisation, when there is no any histopathological changes and arthritis symptoms. Flow cytometry and immunofluorescence staining indicated that the proportion of pre-OCs were significantly increased in bone marrow after day 25 with the presence of BME. At day 25, accompanied by presence of BME and increased pre-OCs, the number of trabecular bone was significantly diminished as compared with those at day 20 and reached its lowest number at day 35. We then examined the transcription of several pro-inflammatory cytokines and chemokines related to OCs differentiation, migration and activation, such as RANKL, IL-17, TNF α , CCL3, CCL4, CCL12, CCR5 by Real-time PCR. The most prominent RANKL

change was observed at day 35. IL-17 and TNF α mRNA were elevated from day 25, reaching a peak at day 28 and thereafter gradually decreasing. Expression of CCL3 and CCL12 were only higher at day 28 and day 25, respectively, while there was no significant change in CCR5 and CCL4 mRNA in the bone marrow. The proportion of T cells and monocytes in bone marrow were significantly higher from day 25 to day 45. No differences in B cells and plasma cells were detectable at any time points. Bone marrow cells from the presence of BME showed significantly increased ability to formation OCs *in vitro*.

Conclusions: BME precede the synovitis and arthritic symptoms during the development of CIA. Accompanied BME appearance, we identified an altered bone microenvironment that favours OCs differentiation and survival in CIA mice. We proposed that BME linked to a unique "osteoclastic environment" in CIA disease progression. These findings provide a new perspective for comprehending the development of erosions in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4189

AB0139 INVESTIGATION OF PREVOTELLA COPRI FROM RHEUMATOID ARTHRITIS PATIENTS

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Background: We have previously reported some of the rheumatoid arthritis (RA) patients had *Prevotella copri* in the intestine. By using germ-free (GF) SKG mice, we also showed that *Prevotella*-dominated gut microbiota contribute to the development of arthritis¹⁾. However, *P. copri* itself has not been isolated from RA patients and their molecular biology was unknown.

Objectives: Firstly, we planned to evaluate the intestinal microbiota in RA patients before and after the treatment. Second, we isolated *P. copri* strains from RA patients and healthy controls (HCs) and analysed whether RA patients-derived *P. copri* expanded in the intestine of GF mice.

Methods: We first examined whether RA patients have altered composition of microbiota. All the patients were diagnosed according to the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria for RA. We collected faecal samples from 55 RA patients (61.5 $\pm$ 9.5 years, mean ages $\pm$ SD) and 33 HCs (56.2 $\pm$ 8.2 years) to investigate the microbiota by 16S rRNA-based deep sequence technique. We also analysed bacterial counts of *Prevotella* and *Bacteroides fragilis* by qPCR method. Moreover, we isolated *P. copri* from faecal contents of RA patients and HCs. GF mice were inoculated with *P. copri* from RA patients and HCs for further analysis.

Results: We found that 34.5% (19/55) of RA patients and 18.1% (6/33) of healthy controls have relatively high abundance of *Prevotella* (>4%) in the intestine. These results were compatible with our previous observations. When we focused on the patients who harboured high abundance of *Prevotella* in the gut, *Prevotella/B. fragilis* ratio was decreased after the treatment. The mean *Prevotella/B. fragilis* ratio were changed from 1.28 to 0.75 ($p=0.08$). Further analyses revealed that RA patients-derived *P. copri* successfully colonised to GF-mice and induced Th17 cells in the large intestine.

Conclusions: We found that alternation of microbiota composition was observed after the RA treatment. Moreover, we successfully isolated *P. copri* from RA patients and HCs. RA patients-derived *P. copri* efficiently expanded in the intestine of GF mice.

REFERENCE:

- [1] Maeda Y, et al. Dysbiosis contributes to arthritis development via activation of autoreactive T cells in the intestine. Arthritis Rheumatol 2016;68 (11):2646–2661.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5350

AB0140 THE ROLE OF RAF KINASE INHIBITORY PROTEIN IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune inflammatory disease of the joints and is characterised by immune cell infiltration, synovial hyperplasia, and destruction of cartilage and underlying bone¹. Raf kinase inhibitory protein