Conclusions: Several studies reported the potential of BIO withdrawing, spacing or reducing in the patients with RA who reached remission^{3, 5}. All cases in spacing and withdrawing group have shown DAS28-4ESR<2.6 in this study, however, 50% (5/10 cases) in withdrawing group have re-flare and shown the radiological joint destruction. Spacing or reducing of BIO may have potential to maintain the remission of RA and prevent the joint destruction. Withdrawing of BIO after even sustained deeper remission may be difficult to keep real remission.

REFERENCES:

- [1] O'Dell JR. *Arthritis Rheum* 2002;46:283–85.
- [2] Smolen JS, et al. *Ann Rheum Dis* 2017;76:960–77.
- [3] Tanaka Y, et al. *Ann Rheum Dis* 2015;74:389–95.
- [4] Takeuchi T, et al. *Ann Rheum Dis* 2014;73:536–43.
- [5] Fautrel B, et al. *Ann Rheum Dis* 2016;75:59–67.

Acknowledgements:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2016

FRIDAY, 15 JUNE 2018

Spondyloarthritis – etiology, pathogenesis and animal models

FRI0148 A STUDY OF MICROBIAL TRANSLOCATION IN AN ANIMAL MODEL OF SPONDYLOARTHRITIS

M. Asquith¹, M. Schleisman¹, S. Davin¹, L. Karstens², J.T. Rosenbaum¹. ¹Division of Arthritis and Rheumatic Diseases; ²Department of Medical Informatics and Clinical Epidemiology, Oregon Health and Science University, Portland, USA

Background: The intestinal microbiota is believed to have a central role in SpA pathogenesis. However, the mechanism through which enteric microbes contribute to peripheral inflammation remains enigmatic.

Objectives: The primary objective of this study was to determine whether microbial translocation can be observed to extra-intestinal tissues in the HLA-B27/β2m transgenic rat – a foremost translational model of spondyloarthropathy. Moreover, since an arthritis phenotype only presents in less than half of HLA-B27/β2m transgenic animals, we could examine whether microbiota composition between transgenic animals with and without arthritic disease.

Methods: Intestinal tissue (cecal contents), mesenteric lymph nodes (MLN), spleen, serum, liver, lung, ankle joint and eye were collected from age matched (20–24wk old) HLA-B27/β2m transgenic rats with or without arthritis and WT controls (n=20–45 per group). DNA was extracted and the 16 s rRNA V4 region amplified according to the standard Earth Microbiome Project protocol. Extraction blanks were run with each tissue to control for environmental contamination. Sequencing data (generated by Illumina MiSeq) was first processed using the SourceTracker algorithm to identify and remove contaminant sequences. Remaining reads were run through the DADA2 pipeline implemented in QIIME2.

Results: Our study of microbial translocation revealed a number of striking observations.

Firstly 16 s rRNA was detected at all tissue sites examined. Second, rather than observing a limited number of species, a highly polymicrobial and intestinal DNA signature was observed in all tissue sites examined. This observation was independent of genotype or disease state. The number of total reads in each tissue was highest in cecum as anticipated (approx. 1 00 000 reads) with the yield from other tissues roughly an order of magnitude lower.

The most abundant species in joint tissue included *Prevotella* spp. *Prevotella shahii* and *Prevotella stercorea*, *Roseburia faecis* and *Muribaculum intestinale*. The microbe *Blautia obeum*, a close relative of [*Ruminococcus*] gnavus within the same genus was also found in joint tissue. This of interest since this microbe has recently been associated with disease activity in SpA patients.

Interestingly an arthritis phenotype was strongly associated with a loss of intestinal bacterium *Eubacterium Oxidoreducens*. This is a flavone metabolising bacterium and supports previous metabolomic studies in which we have shown flavone compounds are greatly over-represented in the HLA-B27/β2m transgenic rats vs WT controls.

Conclusions: We propose translocation of microbes/microbial products from the gut to extra-intestinal tissues may be a contributory mechanism to SpA pathogenesis, although alone is not sufficient to elicit inflammatory disease. Specific changes in microbial community DNA profile in the gut or elsewhere may serve as useful biomarkers of disease state in either patient populations or disease models. This approach may yield useful candidates for further study such as *Eubacterium Oxidoreducens*. Future studies will verify our findings using PCR-independent methods.

Acknowledgements: JMA and JTR are supported by the Spondylitis Association of America and the Rheumatology Research Foundation. JTR also receives support from the William and Mary Bauman Foundation, the Stan and Madelle Rose-nfeld Family Trust and Research to Prevent Blindness.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7487

FRI0149 INFLAMMATION INTENSITY-DEPENDENT EXPRESSION OF OSTEOINDUCTIVE WNT PROTEINS IS CRITICAL FOR ECTOPIC NEW BONE FORMATION IN ANKYLOSING SPONDYLITIS

H. Liu, X. Li, J. Wang. *Spine Surgery, The first affiliated hospital of Sun Yat-sen University, Guangzhou, China*

Objectives: To investigate the molecular mechanism underlying the inflammation-related ectopic new bone formation in ankylosing spondylitis (AS).

Methods: Spinal tissues and sera were collected from patients or normal volunteers to detect the expression of Wnt proteins. An *in vitro* cell culture system mimicking the local inflammatory microenvironment of bone-forming sites was established to study the relationship between inflammation and Wnt expression, the regulatory mechanism of inflammation-induced Wnt expression and the role of Wnt signalling in new bone formation. A modified collagen-induced arthritis (mCIA) and a proteoglycan-induced spondylitis (PGIS) animal model were used to confirm the key findings *in vivo*.

Results: The levels of osteoinductive Wnt proteins were obviously increased in the sera and spinal ligament tissues of patients with AS. Only constitutive low-intensity TNF-α stimulation, but not short-term or high-intensity TNF-α stimulation, induced persistent expression of osteoinductive Wnt proteins and subsequent bone formation through NF-κB (p65) and JNK/AP-1 (c-Jun) signalling pathways. Furthermore, inhibition of either Wnt/β-catenin or Wnt/PKCδ pathway significantly suppressed new bone formation. The increased expression of Wnt proteins was confirmed in both mCIA and PGIS models. A kyphotic and ankylosing phenotype of the spine was observed during long-term observation in mCIA model. Inhibition of either Wnt/β-catenin or Wnt/PKCδ signalling pathway significantly reduced the incidence and severity of this phenotype.

Conclusions: Inflammation intensity-dependent expression of osteoinductive Wnt proteins is a key link between inflammation and ectopic new bone formation in AS. Activation of both canonical Wnt/β-catenin and noncanonical Wnt/PKCδ pathways is required for inflammation-induced new bone formation.

Abstract FRI0149 – Figure 1. (A) IHC staining of Wnt proteins in spinal tissues from patients with AS and DS. (B) ELISA analysis of Wnts expression in RAW cells subject to different pattern of TNF-α stimulation. (C) Alizarin red staining of MC3T3 cells stimulated with CM produced from Raw cells transfected with Wnt siRNAs. (D) Site-directed mutagenesis analysis of the Wnt3a promoter. (E) MicroCT images of the spines and hind paws of the mCIA mice. (F) Immunohistological staining of Wnt3a, Wnt5a and Wnt7b in