through upregulating cellular activities involving iNOS-presenting macrophages and B cell receptor signaling, which may be associated with the pathogenesis of *P.g.*-triggered RA.

REFERENCES:

- [1] Jennings M, Marklein B, Ytterberg J, et al. Bacterial citrullinated epitopes generated by *Porphyromonas gingivalis* infection—a missing link for ACPA production. *Ann Rheum Dis* 2020;79:1194–202. doi:10.1136/annrheumdis-2019-216919

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3998

POS0403

RISK FACTORS FOR PROGRESSION OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: REASSURING IMPACT OF METHOTREXATE

C. Lucas¹, A. Tremblay¹, S. Jouneau², A. Perdriger¹. ¹CHU, Rheumatology, Rennes, France; ²CHU, Pneumology, Rennes, France

Background: Factors associated with rheumatoid arthritis-associated interstitial lung disease (RA-ILD) progression and prognosis are not well identified, especially the impact of methotrexate.

Objectives: Identify risk factors of ILD progression in RA-ILD patients in a longitudinal study.

Methods: RA patients with ILD confirmed in 2 high resolution computed tomography (HRCT) chest scans spaced at least 6 months apart (T0: date of the first HRCT chest scan describing ILD; Tx: date of the last HRCT chest scan available) were consecutively included in this retrospective multi-centric study from 2010 to 2020. HRCT chest scans were analyzed for each patient at T0 and Tx by 2 independent radiologists to determine ILD pattern (definite UIP, probable UIP, indeterminate UIP, non-UIP) and progression during the follow-up including variation of the fibrosis score (aggravated or non-aggravated). Characteristics of patients (demographic-clinical-biological findings, respiratory function tests, and treatments exposure) at ILD diagnosis and during the follow-up (T0-Tx) were analyzed as potential determinants of ILD progression through multivariable logistic regression analysis. Overall survival was analyzed using Kaplan-Meier method.

Results: 74 RA-ILD patients were included. During a mean duration between T0-Tx of 2.8 years $\pm$ 2.4, 26 patients (35%) had ILD progression. Thirty-three patients (45%) were treated by methotrexate at ILD diagnosis (T0) and 29 of them (39%) continued methotrexate during T0-Tx. Logistic regression in multivariate analysis revealed that a treatment by methotrexate at ILD diagnosis was protective against ILD progression (OR=0.14 [0.04-0.52]; $p=0.0031$). Non-UIP pattern at ILD diagnosis was also protective against ILD progression (OR=0.09 [0.02-0.36]; $p=0.0005$). The follow-up for survival analysis was 5.1 years $\pm$ 2.9. Thirty-three patients (31%) died, and the 3-year survival rate was 80%. Survival was better for non-aggravated ILD patients (HR=3.5 [1.46-8.4]; $p=0.004$) and for patients treated by methotrexate during T0-Tx (HR= 0.36 [0.15-0.84]; $p=0.018$) and worse for definite UIP patterns (HR=2.570 [1.078-6.128]; $p=0.0332$).

Conclusion: In RA-ILD patients, non-UIP pattern and methotrexate treatment are associated with better ILD evolution and prognosis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.4157

Spondyloarthritis - aetiology, pathogenesis and animal models

POS0404

VOLUNTARY WHEEL RUNNING MODEL IN MICE TO MECHANICALLY STIMULATE THE ENTESIS OF THE ACHILLES TENDON

A. Briolay¹, S. Delplace², F. Duboeuf³, O. Peyruchaud³, D. Magne¹, L. Brizuela¹, C. Bougault¹. ¹Université Claude Bernard Lyon 1, CNRS UMR 5246, Lyon, France; ²Université du Littoral-Côte d'Opale, ULR 4490, Boulogne/Mer, France; ³Faculté de Médecine Lyon Est, INSERM U1033, Lyon, France

Background: Excessive bone formation in the entheses is one of the features of peripheral spondyloarthritis. Biomechanical stress is proposed to occupy a central place in spondyloarthritis pathophysiology, but the precise molecular and cellular mechanisms underlying the pathological response of the entheses are still largely unknown [1]. Besides, physical therapy and exercise are recommended as non-pharmacologic therapies for patients. We focused on the effect of exercising on entheses ossification.

Objectives: We aimed to develop and characterize an *in vivo* model in mice to study the impact of mechanical stimulation on the entheses of the Achilles tendon.

Methods: DBA/1 mice were subjected to voluntary running exercise by the use of activity wheels for two weeks, and compared to mice housed in standard conditions (n=17 per group). The running performances were recorded.

Figure 1. Expression level of the mechanosensitive gene Sclerostin (*Sost*). It dropped in response to exercise in enthesal tissues, but not in long bones, revealing a tissue-specific response to mechanical stimulation.

mRNAs were extracted from the long bones (flushed tibia and femur) and the ankles' entheses for real-time PCR analysis. μ CT was performed on the femurs. Alkaline phosphatase activity was detected by histology on the anchorage of the Achilles tendon to the calcaneum, and by enzymatic assay in serum samples. Luminex analysis was also conducted on serum samples for IL-6 and IL-8/Kc detection.

Results: Free access to the activity wheel resulted in a running exercise of 5.5 ± 0.8 km/day (approximately 80 km in total) at 14.5 ± 0.5 m/min. No effect was detected on the femur architecture by μ CT. Sclerostin (*Sost*) gene expression was monitored as a mechanosensitive marker. Its expression was expectedly reduced by half in enthesal tissues, but no modulation was observed in long bones (Figure 1). Similarly, exercise-induced regulation of *Osterix* and *Runx2* expressions was observed only in entheses samples. This tissue-specific pattern was also verified for key genes of the sphingosine-1 phosphate metabolic pathway, which we recently implicated in spondyloarthritis pathophysiology [2]. The *in situ* staining of alkaline phosphatase activity suggested the presence of more positive cells in the anchorage of Achilles tendon of running mice, compared to control ones. However, alkaline phosphatase activity in serum samples and its gene expression in rough tissue extracts were unchanged. No inflammatory response was detected as IL-8/Kc serum levels were similar in the control and the exercising group (59 ± 14 vs 57 ± 14 pg/mL). In addition, IL-6 was not detected in the serum and its expression was very faint and constant in the tissue extracts.

Conclusion: This work is still in progress for a more complete characterization of the model. We believe that this experimental design will be useful to study the role of mechanical stimulation specifically in the entheses and that it can help to better understand the spondyloarthritis pathophysiology.

REFERENCES:

- [1] Cambré, et al. *Nat Commun*, 2018; [2] El Jamal, et al. *J Bone Miner Res*, 2019

Acknowledgements: Société Arthritis R&D (2020)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.833

POS0405

GENETIC VARIANTS WITHIN PSORIATIC ARTHRITIS (PsA)-WEIGHTED GENES FBXL19 AND HLA-B*39 MAY SERVE AS A POTENTIAL LINK BETWEEN PsA AND OBESITY

C. Welsh¹, T. Burry¹, Q. Li¹, A. Dohey¹, D. Codner¹, V. Chandran^{2,3,4}, D. D. Gladman^{3,4}, D. O'Rielly¹, P. Rahman². ¹Memorial University, Genetics, St. John's, Canada; ²Memorial University, Medicine, St. John's, Canada; ³Krembil Research Institute, UHN, Toronto, Canada; ⁴University of Toronto, Rheumatology, Toronto, Canada

Background: PsA patients have been observed to have a higher body mass index (BMI) compared to individuals with a similar disease (e.g., rheumatoid arthritis) or healthy controls¹. Approximately 45% of PsA patients are considered obese with BMI's exceeding 30 kg/m², and these patients have more severe articular disease and lower response to therapy². A recent mendelian randomization study noted that higher BMI leads to higher risk of psoriasis when using genetic variants as instrumental variables for BMI³.

Objectives: To determine if known PsA-weighted genetic variants are overrepresented in an obese population.