were stimulated on the same day of isolation. Both moDCs and mDCs were pre-treated with Tofacitinib and then stimulated with either lipopolysaccharide (LPS) or combination of LPS with IFN- γ for 4 hours. Cytokines were measured using enzyme-linked immunosorbent assay (ELISA) and gene expression was assessed using quantitative polymerase chain reaction (qPCR).

Results: Treatment of both mDCs and moDCs with Tofacitinib led to a decreased mRNA expression of IL-12 p40 (*IL12B*) in the presence of TLR4 and IFN γ co-stimulation. The decreased *IL12B* mRNA expression also resulted in lower production of IL-12 p40 and IL-23 proteins in mDCs.

Conclusion: In this work, we demonstrated for the first time that Tofacitinib can suppress the production of IL-23/IL-12 p40 subunit in mDCs, upon the condition that an active type II IFN signalling is also present in these cells. This observation indicates that specific factors, such as endogenous IFN- γ levels in the serum of PsA patients, can possibly predict differential responses to Tofacitinib treatment.

References:

- [1] Gaffen SL, et al. The IL-23-IL-17 immune axis: from mechanisms to therapeutic testing. *Nat Rev Immunol.* 2014 Sep;14(9):585-600
- [2] Bravo A, Kavanaugh A. Bedside to bench: defining the immunopathogenesis of psoriatic arthritis. *Nat Rev Rheumatol.* 2019 Nov;15(11):645-656
- [3] Floss DM, et al. Insights into IL-23 biology: From structure to function. *Cytokine Growth Factor Rev.* 2015 Oct;26(5):569-78
- [4] Berekmeri A, et al. Tofacitinib for the treatment of psoriasis and psoriatic arthritis. *Expert Rev Clin Immunol.* 2018 Sep;14(9):719-730
- [5] T Virtanen E, et al. Selective JAKinibs: Prospects in Inflammatory and Auto-immune Diseases. *BioDrugs.* 2019 Feb;33(1):15-32

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.3307

OA, aetiology, pathology and animal models

AB0063

AGING CARTILAGE IN WILD-TYPE MICE: AN OBSERVATIONAL STUDY

J. Akoum¹, K. Tahiri¹, F. Etienne¹, M. T. Corvol¹, F. Rannou^{1,2}, C. Nguyen^{1,2}

¹Université de Paris - UFR Mathématiques et Informatique, Paris, France;

²Hospital Cochin, Rheumatology Institute, Rehabilitation Department, Paris, France

Background: Many animal models of osteoarthritis (OA) have been used to study the pathogenesis of cartilage degeneration¹. In mice, spontaneous OA can occur in wild-type or genetically modified animals. The first report of spontaneous OA developing in wild-type mice was published in 1956² and changes affecting the knee joint were further related to OA by using ultrastructural-histochemical analyses. However, a quantitative assessment of age-related evolution of OA-type cartilage lesions is lacking. The OA Research Society International (OARSI) grading score was adapted to semi-quantify histopathological changes occurring in OA animal models, including mice³. The OARSI score has been used to describe changes occurring in induced or genetic OA mouse models but not to describe spontaneous age-related evolution of OA-type cartilage lesions in wild-type mice.

Objectives: We aimed to describe the spontaneous evolution of age-related changes affecting knee joint articular cartilage, walking speed and a serum biomarker of cartilage remodeling in C57BL/6 wild-type male mice.

Methods: Histological changes were assessed by the OARSI score in newborn, 1-week- and 1-, 3-, 6-, 9- and 12-month-old C57BL/6 wild-type male mice, walking speed by the Locotronic system, and serum C-terminal telopeptide of type II collagen (CTX-II) content by ELISA in 1-, 3-, 6-, and 9-month-old C57BL/6 wild-type male mice.

Results: Mean (SD) OARSI score increased from 0.2(0.3) to 1.3(0.6) ($p=0.03$) between 1 and 3 months of age and from 1.3(0.6) to 3.3(0.6) ($p=0.04$) between 3 and 6 months of age. Mean walking speed was stable between 1 and 6 months of age but decreased from 11.4(1.8) to 3.2(0.8) cm.s⁻¹ ($p=0.03$) between 6 and 9 months of age. Serum CTX-II content was maximal at 1 month of age, then decreased from 12.2(8.5) to 2.4(8.4) pg/ml ($p=0.02$) between 1 and 3 months of age, remaining low and stable thereafter.

Conclusion: C57BL/6 wild-type male mice showed continuously increasing osteoarthritic changes but delayed decreasing walking speed with age. These variations were maximal between 3 and 9 months of age. Maximal serum CTX-II content preceded these changes.

References:

- [1] McCoy AM. Animal Models of Osteoarthritis: Comparisons and Key Considerations. *Vet Pathol.* 2015;52(5):803-18.
- [2] Sokoloff L. Natural history of degenerative joint disease in small laboratory animals. I. Pathological anatomy of degenerative joint disease in mice. *AMA Arch Pathol.* 1956;62(2):118-28.

- [3] Glasson SS. The OARSI histopathology initiative - recommendations for histological assessments of osteoarthritis in the mouse. *Osteoarthritis Cartilage.* 2010;18 Suppl 3:S17-23.

Table 1. Evolution of cartilage changes, walking speed and serum C-terminal telopeptide of type II collagen (CTX-II) concentrations in wild-type C57BL/6 male mice.

Age	New-born	1 week	1 month	3 months	6 months	9 months	12 months
OARSI score (0 to 6)	0.0 (0.0)	0.0 (0.0)	0.2 (0.3)	1.3 (0.6)*	3.3 (0.6)*	3.7 (0.6)	4.3 (0.6)
Walking speed (cm.s⁻¹)	-	-	10.5 (1.5)	11.3 (4.3)	11.4 (1.8)	3.2 (0.8)*	-
CTX-II concentrations (pg/ml)	-	-	12.2 (8.5)	2.4 (8.4)*	1.1 (4.0)	4.0 (3.8)	-

N ≥ 3 per timepoint. All results are means (standard deviation). * $p<0.05$ as compared to the previous timepoint using the non-parametric Mann-Whitney U-test.

Figure 1. (A) New born, 1-week- and 1-, 3-, 6-, 9- and 12-month-old wild-type C57BL/6 male mice (N=3 per timepoint) knees were evaluated for cartilage changes following OARSI recommended guidelines by 3 independent readers. Each point represents the mean of OARSI score per mice as scored by 3 independent readers. **(B)** 1-, 3-, 6- and 9-month-old wild-type C57BL/6 male mice were evaluated for walking speed using the Locotronic® system. Each point represents the mean of 3 measures of walking speed per mice. All results are means (SD). * $p<0.05$ as compared to the previous timepoint using the non-parametric Mann-Whitney U-test.

Disclosure of Interests: Joulmar Akoum: None declared, Khadija Tahiri: None declared, François Etienne: None declared, Marie-Thérèse Corvol: None declared, François Rannou Grant/research support from: Pierre Fabre, Fidia, MSD, Pfizer, Bone Therapeutics, Expanscience, Grunenthal, Thuasne, Genévrier, Fondation Arthritis, Consultant of: Pierre Fabre, Fidia, MSD, Pfizer, Bone Therapeutics, Expanscience, Grunenthal, Thuasne, Genévrier, Speakers bureau: Pierre Fabre, Fidia, MSD, Pfizer, Bone Therapeutics, Expanscience, Grunenthal, Thuasne, Christelle Nguyen: None declared

DOI: 10.1136/annrheumdis-2020-eular.5989

AB0064

CHANGES IN THE VASCULAR ENDOTHELIAL GROWTH FACTOR A (VEGFA) SPLICING AXIS IN HUMAN SYNOVIUM ARE RELATED TO INFLAMMATION IN ARTHRITIS

D. Amanitis^{1,2}, S. Shahtaheri^{2,3}, D. Daniel McWilliams^{2,3}, N. Beazley-Long¹, D. Walsh^{2,3}, L. Donaldson^{1,2}. ¹University of Nottingham, School of Life Sciences, Nottingham, United Kingdom; ²University of Nottingham, Pain Centre Versus Arthritis, Nottingham, United Kingdom; ³University of Nottingham, School of Medicine, Academic Rheumatology, Nottingham, United Kingdom

Background: VEGF-A is a key regulator of rheumatoid (RA) and osteoarthritis (OA). During articular inflammation in OA and RA there is increased synovial angiogenesis and upregulation of angiogenic growth factors such as VEGF-A. VEGF-A comprises two splice variant families, VEGF-A_{xxx}a and VEGF-A_{xxx}b (xxx represents the number of amino acids, from 121 to 206), resulting from alternative splice site selection in exon 8. This site selection is controlled by Serine/Arginine Rich Splicing Factor Kinase 1 (SRPK1), which phosphorylates Serine/Arginine Rich Splicing Factor 1 (SRSF1), inducing it to translocate to the nucleus. In most normal tissues, VEGF-A_{xxx}b isoforms predominate, with anti-nociceptive and anti-angiogenic functions. In contrast, in pathological conditions such as inflammation and solid tumours, VEGF-A_{xxx}a isoforms predominate, with pro-nociceptive and pro-angiogenic functions. VEGF-A has been proposed as