Ethical approval NR: S-096/2016.

Results: The intake of the FFA palmitate by CD8s was higher in all patients groups than in HC ($p < 0.05$). In all three diseases' stimulated CD8s, unlike in the HC group, the expression of GPR84 was inversely correlating to the expression of CD69 (Spearman $r < -0.62$). In patient's stimulated CD8s the expression of GPR84 tended to be lower in RA and PSA effector memory (EM) CD8s. In RA and HC the expression of FABP4 tended to be lower in the naive CD8+ subset when compared to the effector subset. HC naive and effector CD8+ subsets had a higher expression of CD36 than in the patient groups. In RA and SPA patients the expression of FAT correlated with clinical variables. In RA DAS28 and CRP inversely correlated with CD36 (MFI), and disease duration with FABP4 as well. In SPA CRP and BASDAI inversely correlated with FABP4 while disease duration had a negative correlation with CD36 (MFI). GPR84 (MFI) had an inverted relationship to BASDAI. While the BMI was directly correlated with the expression of CD36 in RA, this relationship was inverted in SPA.

Conclusion: A high free fatty acid uptake seems to characterize autoimmune arthritis CD8+ T cells. The gain of effector functions appears to be connected to changes in the expression of different fatty acid transporters on the surface of CD8+ T cells. The correlation between the expression of fatty acid transporters and clinical parameters (specially disease activity scores) in RA and SPA suggests that they could potentially be used as biomarkers for disease activity and progression.

Acknowledgements: We thank all the individuals involved in the study for their participation.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3069

Innate immunity in rheumatic diseases

AB0029

THE METABOLIC HIERARCHY OF IMMUNE PROCESSES IN HUMAN MONOCYTES

P.L. Krauß¹, F. Buttgerit¹, T. Gaber¹, M. Pfeifferberger¹, Y. Chen¹, T. Buttgerit².
¹Charité Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany; ²Charité Universitätsmedizin Berlin, Dermatology, Venerology, and Allergology, Berlin, Germany

Background: At sites of inflammation, monocytes carry out specific immunological functions while facing challenging bioenergetic restrictions.

Objectives: Here, we investigated the potential of human monocytes to adapt under conditions of reduced energy supply by gradually inhibiting oxidative phosphorylation (OXPHOS) under glucose free conditions.

Methods: We modelled this reduced energy supply with myxothiazol, an inhibitor of mitochondrial respiration, at 0, 2 and 4 pmol/10⁶ cells to decrease mitochondrial ATP production for 0%, 25% and 66% under glucose free conditions. For the three energy levels, we assessed (i) phagocytosis of FITC-labelled *E.coli* using flow cytometry, (ii) production of reactive oxygen species (ROS) through NADPH oxidase (NOX) as determined by VAS2870-sensitive OCR using a Clark-type electrode, (iii) ATP generation and steady state level using a Clark-type electrode and luminometric assessment (iv) expression of surface activation markers CD16, CD80, CD11b, HLA-DR and (v) production of the inflammatory cytokines IL-1 β , IL-6 and TNF- α using flow cytometry in peripheral blood-derived human monocytes with and without LPS-stimulation.

Results: As a prerequisite for our study, we demonstrate that human monocytes survived strong inhibition of mitochondrial respiration without any sign of apoptosis as determined by flow cytometry. As a result of the inhibition of OXPHOS, we demonstrate a reduction of VAS2870-sensitive OCR (ROS production through NOX), ATPase-dependent OCR and ATP steady-state levels. Focusing on immune function, we observed that phagocytosis and the production of IL-6 were the least sensitive to reduced energy supply while surface expression of CD11b, HLA-DR, production of TNF- α and IL-1 β were most affected by inhibition of OXPHOS.

Conclusion: Our data demonstrate an energy-dependent hierarchy of immune functions in monocytes, which may represent a potential therapeutic target in monocyte-mediated inflammatory diseases.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.794

AB0030

BETA BOSWELLIC ACID BLOCKS INNATE IMMUNE RESPONSES IN MULTIPLE OA JOINT CELLS

E. Franco-Trepát¹, A. Lois-Iglesias¹, A. Alonso-Pérez¹, M. Guillán-Fresco¹, M. López-Fagúndez¹, J. P. Cerón-Carrasco², A. Pazos-Pérez¹, A. Crespo-Golmar¹, A. Jorge-Mora¹, S. Belén Bravo³, R. Gómez¹.
¹Institute IDIS, Musculoskeletal Pathology Group, Santiago de Compostela, Spain; ²Universidad Católica de Murcia (UCAM), Bioinformatics and High Performance Computing (BIO-HPC), Murcia, Spain; ³Institute IDIS, Proteomics Unit, Santiago de Compostela, Spain

Background: Osteoarthritis (OA) incidence has skyrocketed in the last decade and yet a definitive treatment has still to be found. This worldwide disease is depriving our society from their life quality and has become a grave economic burden.

Research on anti-inflammatory tools has been done on traditional Asian medicine. Boswellic acid is a plant-derived molecule from the *Boswellia* species that has shown to prevent cartilage loss in an OA mouse model[1]. However, the specific mechanism of action is still unclear. The activation of innate immune receptors, such Toll-like receptor 4 (TLR4) has been involved in chondrocyte-mediated inflammatory responses and OA development. Although, boswellic acid has shown an inhibitory effect on TLR4-mediated inflammatory responses little is known about its role on TLR4-mediated chondrocyte inflammatory and catabolic responses.

Objectives: Determine the ability of beta boswellic acid (BBA) to block TLR4-mediated innate immune responses in chondrocytes and synoviocytes.

Methods: *In silico*

The binding affinity of beta boswellic acid (BBA) to TLR4 complex signalling was determined by optimized docking algorithm in the BIO-HPC Research Group facilities.

In vitro

Cellular proteome and secretome profiling (LC-MALDI/TOFF) was used to study inflammatory pathways induced by the agonist of TLR4 (LPS [100ng/ml]) and IL1R (IL1 β [0.1ng/ml]). The effect of BBA on TLR4-mediated innate immune responses was determined by RT-PCR, Western Blot and ELISA in primary human OA chondrocytes (hOC), murine ATDC5 chondrocytes, human synoviocytes (SW982) and primary human osteoblasts (hOB). Cell viability was tested using the methyl-thiazolyl-tetrazolium (MTT) reagent. Nitric oxide production in cell culture media was assessed by Griess reaction. Green Malachite Assay was used to semi-quantify the whole phosphoproteome.

Ethics

This study was approved by the CEIC (CAEIG 2014/310).

Results: Cellular proteome and secretome profiling validated the activation of TLR4 and IL1R signalling by LPS and IL1 β ligands and revealed an enrichment in innate immune responses (NF- κ B, NLRP3, MMPs, Interleukins, etc).

Non-toxic doses of BBA [0.5-1000nM] prevented the activation of TLR4 in multiple articular joint cells and inhibited TLR4 & IL1R-dependant innate immune responses at the mRNA and protein level such as inflammatory factors IL6, NOS2, COX2, LCN2, MMP1, -3, -9, -13 and ADAMTS4, among others. Furthermore, NF- κ B/IKB α and NLRP3/PYCARD/IL1 β axis were also severely inhibited after BBA treatment. Moreover, these results were validated by *in silico* docking analysis that showed BBA interacted with TLR4/NF- κ B.

Conclusion: We prove that BBA inhibit TLR4 & IL1R -dependant innate immune responses in multiple human joint cells (Figure 1). We show that NF- κ B & NLRP3 signalling, both associated to OA, are blocked (mRNA and protein) after BBA treatment (Figure 1).

Our data support previous studies showing the prevention of cartilage loss in an OA animal models by BBA might come from its ability to inhibit TLR4 signalling. In the clinical practice of rheumatologists, *Boswellia Serrata* could be a useful nutraceutical to manage OA inflammation due to its content in BBA.

Figure 1.

REFERENCES:

- [1] Wang, Q.; Pan, X.; Wong, H.H.; Wagner, C.A.; Lahey, L.J.; Robinson, W.H.; Sokolove, J. Oral and topical boswellic acid attenuates mouse osteoarthritis. *Osteoarthritis Cartil.* 2014, 22, 128–132, doi:10.1016/j.joca.2013.10.012.

Acknowledgements: Eloi Franco-Trepát and Ana Lois-Iglesias contributed equally to this work.

This research has been funded by the non-profit FER (Fundación Española de Reumatología /Spanish Foundation of Rheumatology) through the project "Búsqueda de nuevos fármacos bloqueantes de la inflamación asociada a TLR4 en condrocitos humanos artrósicos".

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1889