Innate immunity in rheumatic diseases

**AB0029**

THE METABOLIC HIERARCHY OF IMMUNE PROCESSES IN HUMAN MONOCYTES

P. L. Kraus1, F. Buttgereit1, T. Gaber1, M. Pfeifenberger1, Y. Chen1, T. Buttgereit1

1Charite Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany; 2Charite 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/10^6 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 electrode and luminometric assessment (iii) expression of surfaceactivation markers using flow cytometry, (iv) production of the inflammatory cytokines IL-6 and TNF-α, IL-1β, IL-23, IL-10 and IL-13 using ELISA. Additionally, we assessed (v) production of the inflammatory cytokines IL-6, TNF-α, IL-1β, IL-10 and IL-13 using ELISA.

**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 observed that phagocytosis and the production of IL-6 were the least sensitive to reduced energy supply while surface expression of CD11b, HLA-DR and production of the inflammatory cytokines IL-1β, IL-6 and TNF-α using flow cytometry in peripheral blood-derived human monocytes with and without LPS-stimulation.

**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-Trepat1, A. Lopez-Iglesias1, A. Alonso-Pérez1, M. Guillán-Fresco1, M. López-Fagúndez2, J. P. Cerón-Carrasco1, A. Pazos-Pérez1, A. Crespo-Golmar1, A. Jorge-Mora1, S. Belén Bravo1, R. Gómez1, 2Instituto IDIS, Musculoskeletal Pathology Group, Santiago de Compostela, Spain; 3Universidad Católica de Murcia (UCAM), Bioinformatics and High Performance Computing (BIO-HPC), Murcia, Spain; 4Instituto 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.

**Results:** The intake of the FFA palmitate by CD68 was higher in all patients groups than in HC (p < 0.05). In all three diseases’ stimulated CD68, 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 CD68 the expression of GPR84 tended to be lower in RA and PSA effector memory (EM) CD68. In RA and HC the expression of FABP4 tended to be lower in the naive CD68 subset when compared to the effector subset. HC naive and effector CD68 subsets had a higher expression of CD36 than in the patient groups. In RA and SPA patients the expression of F4/80 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 BSDAAL inversely correlated with FABP4 while disease duration had a negative correlation with CD36 (MFI). GPR84 (MFI) had an inverted relationship to BSDAAL. 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 CD68+ 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 CD68+ T cells. The correlation between the expression of fatty acid transporters and clinical parameters (specify 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

**Figure 1.**

**REFERENCES:**


**Acknowledgements:** Eloí Franco-Trepat 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 condroctos humanos artroscópicos.”

**Disclosure of Interests:** None declared

DOI: 10.1136/annrheumdis-2021-eular.1889