the macrophages depended on the elasticity of bacterial cell walls and on the time of their joint cultivation.

Conclusions: LAB and bifidobacteria strains stimulate immunomodulatory cytokines and active oxygen and nitrogen oxides compounds production in macrophages. Strains with a more elastic cell wall according to AFM data demonstrated higher resistance to intracellular digestion in macrophages and higher level of their activation. AFM might be considered as a fast and accurate method to assess parameters of probiotic strains cell wall to predict their beneficial immunomodulatory properties. Further large-scale preclinical research needed for future application in rheumatic diseases treatment and prevention.

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AB0044 HYPER Ig-D SYNDROME TREATMENT WITH HYDROXYCHLOROQUINE

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Background: Hyper IgD syndrome is a minor form of mevalonate kinase deficiency caused by a its gene mutation and considered an auto-inflammatory disease inherited in an autosomal recessive manner, characterised by periodic episodes of fever, arthralgia, lymphadenopathy, skin rash, headaches, and abdominal pain. These attacks can occur spontaneously or be triggered by infections. Treatment options include courses of NSAIDs, steroids, colchicine, statins, I.V immunoglobulin, Cyclosporine, anti-IL-1 agents (anakinra or canakinumab) and anti-TNF antagonist Etanercept, with transient response. To date, there is no report with long term hydroxychloroquine treatment¹⁻³.

Objectives: To report a case of Hyper Ig-D syndrome with multiple recurrent episodes and successful treatment using Hydroxychloroquine alone.

Methods: We report a case of 36-year-old female, presented with a first manifestation at age 35 with fever and extended cellulitis of the left arm treated successfully with antibiotic, rapidly followed with urticarial rash involving the upper side of the body, face and upper limbs migratory type lasting less than 24 hours suspecting allergic reaction. She was under supportive treatment (anti-histaminic and low dose steroids) that improved her condition temporarily. She developed multiple recurrent similar episodes for 7 months with high grade fever up to 39°C, inflammatory polyarthralgia affecting small joints, recurrent left elbow erythematous plaque with few subcutaneous nodules, considered as panniculitis type lesion (Picture-1) along with urticarial rash. Series of tests were undertaken along with skin biopsy.

Results: Biopsy of the lesion showed intense dermal neutrophil infiltrates. CRP fluctuating between 50 to 95 mg/L during the episodes. Neutropenia (1.7 to 1.9), Normal findings for ANA and SSA antibodies, ACE, Lysozyme enzyme, C3 and C4. Other infectious work-up was negative including Quantiferon God test. Protein electrophoresis found hypergammaglobulinemia. The Ig-D level was 263 mg/L and on another occasion 313 mg/L (normal <153 mg/L), the samples were taken during flare up and after recovery. The patient was treated by Colchicine for more than 3 months without beneficial effect. A trial with hydrochochloroquine 400 mg daily brought a progressive improvement with lesser episodes at 3rd month and no recurrences at 6 months. After one year of therapy the patient was symptomless on a lower dose 200 mg daily with completely normalised inflammatory markers.

Conclusions: We conclude that Hyper Ig-D syndrome can be treated by hydroxy-chloroquine. This is the first report in the literature conducting this treatment option that can bring attention for further case by case trials.

Abstract AB0044 – Figure 1

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AB0045 ACTIVATED RNASE L AS A NOVEL DISEASE ACTIVITY BIOMARKER IN PSORIATIC ARTHRITIS

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Background: Almost 60% of psoriasis (PsO) patients with psoriatic arthritis (PsA) are estimated to be untreated, undertreated or/and undiagnosed.¹ Delayed diagnosis leads to permanent joint damage causing major functional decline and diminished quality of life. However, in the absence of diagnostic biomarkers, the diagnosis of psoriatic arthritis is clinical and hence difficult to establish from non-rheumatologists.² Recent studies have demonstrated the upregulation of type I interferon (IFN)–inducible genes in paired peripheral blood cells (PBC) and synovial biopsies of patient with PsA.³ Oligoadenylate synthetases (OAS) are type I IFN-stimulated family of proteins that are activators of the latent Ribonuclease L (RNase L) pathways. The OAS-RNase L system is a potent host antiviral IFN-responsive system that is completely inactive in normal conditions, but once activated mediates a broad array of pro-inflammatory cellular processes.⁴

Objectives:

1. To investigate the role of OAS–RNase L pathway in PsA;
2. To quantify the hypothesised increased OAS–RNase L activity.

Methods: To further explore the gene expression data, we developed a highly sensitive ELISA and fluorescence resonance transfer (FRET) assay to access and compare the RNase L activity in plasma and serum derived from PsA (n=10), PsO (n=10) patients or healthy control donors (n=5).

Results: We found that RNase L activity was 2–3 fold higher in PsO and 3–5 fold in PsA compared to normal control (figure 1). Consistent with the gene expression analysis of upregulated type I IFN inducible genes, we also observed amplification of the downstream pro-inflammatory pathway consisting of RNase L dimer (active) and the produced cleaved RNA, which further induce IFN- β production and other inflammatory signalling.

Abstract AB0045 – Figure 1. RNASEL_Activity

Conclusions: The proportionally increased activation of OAS/RNase L in psoriatic arthritis merits further investigation into this pathway as a potential disease activity biomarker. RNase L is an easily quantifiable enzyme that could categorise disease severity and progression in daily routine lab ordered by primary physician. The timely diagnosis is key to improved function and quality of life in PsA patients.

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AB0046 TOFACITINIB IMPAIRS MONOCYTE-DERIVED DENDRITIC CELL DIFFERENTIATION IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Tofacitinib (Pfizer) is an oral Janus kinase inhibitor, recently approved for the treatment of rheumatoid arthritis (RA). Although its mechanism

of action has been explored in circulating cells, in particular neutrophils and lymphocyte, its effect on dendritic cells development remains still to be elucidate. Monocyte-derived dendritic cells are a subset of inflammatory DC derived from circulating monocytes and have a key role in inflammation and infection.

Objectives: The aim of this project is to evaluate the effect of Tofacitinib on inflammatory monocyte-derived dendritic cells (Mo-DC) from RA and PsA patients, and in particular on the ability of monocyte to differentiate into dendritic cells, an important step in innate immunity.

Methods: Mo-DC were isolated from blood of RA and psoriatic arthritis (PsA) patients by magnetic separation. Monocyte were plated in presence/absence of GM-CSF/IL-4 cocktail for 7 days, to acquire immature dendritic cell phenotype. To evaluate the effect of Tofacitinib on Mo-DC differentiation, monocyte were treated with 1 μ M Tofacitinib (or DMSO as control) for 15 min prior to cytokine stimulation. CD209 (immature DC marker) and CD14 (monocyte marker) were evaluated by flow cytometry in the CD11c positive population. Phagocytosis was investigated by the analysis of dendritic cell uptake of soluble antigens through two different mechanisms: non-specific macropinocytosis (using Lucifer Yellow), and receptor-mediated endocytosis (using DQTM Ovalbumin).¹ Western blot analysis was utilised for analysis of NOX5 and Actin protein expression on the total cell lysate.

Results: The pre-treatment of Mo-DC with Tofacitinib inhibited Mo-DC differentiation in RA and PsA patients, as shown by reduced CD209 surface marker expression, and a mirrored increase of CD14 marker. The decreased ability of monocyte to differentiate into dendritic cells was translated into a function impairment of phagocytic ability, as observed by the decreased uptake of both DQTM Ovalbumin (receptor-mediated endocytosis) and Lucifer Yellow (micropinocytosis) PsA cells treated with Tofacitinib. Low phagocytosis was observed in RA patients. NOX5 has previously been shown to play a key role in Mo-DC differentiation,² therefore we sought to investigate whether Tofacitinib could exert its effect on Mo-DC development through modulating NOX5. NOX5 protein expression was significantly decreased in Mo-DC pre-treated with Tofacitinib in PsA, and to a lesser extent in RA patients.

Conclusions: Together, these observations suggest a novel mechanism of action of Tofacitinib in RA and PsA, by inhibiting Mo-DC development, which may alter migration of DC to the joint and subsequent activation of the immune response.

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Cytokines and inflammatory mediators

AB0047 EXPRESSION OF IFN TYPE I RESPONSIVE GENES IN A CARDIOVASCULAR DISEASE CONTINUUM OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) patients have a prominent increase in cardiovascular disease (CVD) not fully explained by traditional risk factors¹. Interferons type 1 (IFN-I) have been associated with premature CVD in SLE² and are implicated in several aspects of atherosclerosis and acute coronary syndromes³. A subpopulation of RA patients also display a peripheral blood IFN-I signature from 25% to 65%⁴, associated with clinical response to biologics⁵. The IFN-I signature association with CVD in RA remains unclear.

Objectives: To analyse expression of interferon type 1 response genes (ISGs) along a cardiac MRI (CMR) phenotyped CVD continuum in patients with RA.

Methods: PBMC samples from 94 RA patients and 21 healthy controls (HC) were obtained. RA patients were stratified based on CMR into: RA CMRneg (no CVD-