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 DQ^{TM} 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 DQ^{TM} 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-