Macrophages are known to exhibit remarkable phenotypic plasticity and understanding the role of this characteristic in regulating inflammation and pathology remains a major challenge, as does the characterization of factors in the microenvironment such as the synovium that control such macrophage characteristics. Importantly, whether the infiltrating, inflammatory macrophages of the RA ST similarly exhibit such phenotypic plasticity, and whether this occurs during the process of reaching remission, remains to be studied.

**Objectives:** We investigated the phenotypic plasticity of inflammatory synovial macrophages from patients with RA in vitro, investigating their ability to convert from an inflammatory macrophage population into ‘regulatory’ CD206+Mertk+ macrophages. These findings will provide a proof-of-concept as to the utility of these macrophage for a cell-based therapy in resolving inflammation in patients with RA, and will likely extend our understanding of the mechanisms of action of currently used therapeutics.

**Methods:** Synovial fluid (SF) mononuclear cells were obtained from patients with active early RA (<1 year; fulfilling 2010 ACR/EULAR classification criteria). Cryopreserved SFMCs were cultured for 48 hr in the presence of 10 ng/mL interferon (IFN)γ, 50 ng/mL dexamethasone, 10 μg/mL Inflimab, or diluent. Following culture, cells were immunostained and analysed using a Beckman Coulter CytoFLEX flow cytometer and FlowJo software. SF macrophages were characterised by expression of CD14, CD45, CD68 (Figure 1A), and proportions of CD206+Mertk+ macrophages measured.

**Results:** Prior to culture, the CD68+ macrophage populations present in SF were found to be predominantly CD206+Mertk+. After 48 hours of culture, in the absence of any stimulus, there was an increase in proportions of CD206+Mertk+ macrophages. Treatment with either dexamethasone or anti-TNF (Infliximab) resulted in a further increase in proportions of CD206+Mertk+ M2-like macrophages. In contrast, culture with IFNγ induced a reduction in this population. Importantly, we found that the generated CD206+Mertk+ macrophages were phenotypically stable in culture following removal of these differentiating agents.

**Conclusion:** Our findings demonstrate that inflammatory SF cells are indeed able to polarise to regulatory, CD206+Mertk+ macrophages in vitro. The findings provide further mechanistic insights into the basis for the therapeutic benefits of glucocorticoids and TNF inhibitors, as well as providing initial proof-of-concept in the use of regulatory macrophages as a cellular-based therapy or therapeutic target for patients with RA.

**REFERENCES:**

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**Figure 1. Synovial fluid CD68+ macrophage plasticity in vitro.** (A) Gating strategy depicting CD68+CD45+CD14+ CD68+ macrophage determination. (B) Proportions of CD206 and Mertk-expressing SF macrophages after 48hr culture in the presence of 10ng/mL IFNγ, 50ng/mL dexamethasone or 10 μg/mL Inflimab, or absence. Data are representative of 5 individual experiments. Data were analysed by two-way ANOVA followed by Dunnett’s multiple comparison test. *p<0.05.

**Objectives:** To identify common and distinctive novel biomarkers of disease activity in SLE and RA using high-throughput proteomics.

**Methods:** Serum samples from 170 patients, including 100 RA and 70 SLE, were profiled with the disruptive technology “proximity extension assay” from Olink, which analysed the levels of a panel of 92 inflammatory proteins. The methodology involves protein-specific antibodies linked to DNA-encoded tags which are amplified by RT-PCR. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Disease activity score in 28 joints (DAS28) were assessed in SLE and RA patients respectively to characterise the disease status of all patients.

**Results:** Pearson’s correlation studies were performed using molecular information and clinical data to identify biomarkers of disease activity in each disease (FDR<0.05). Gene ontology enrichment analysis were performed to gain insight about the biological meaning of the biomarker signatures.

**Discussion:** SLE patients were characterised by an average SLEDAI of 5.2 (min-max, 0-29) while RA patients exhibited an average DAS28 of 4.6 (min-max, 1.5-78).

**Conclusion:** The levels of five pro-inflammatory mediators were commonly associated with the disease activity status of both diseases such as IL10RB (receptor for IL10, Infln2 and Infln3), CSF1 (macrophage colony-stimulating factor 1 receptor) and SLAMF1 (Signaling lymphocytic activation molecule), TNFRSF9 and OPG (both, tumor receptor factor ligand superfamily members), suggesting a key common role of these molecules in the underlying molecular mechanisms associated with both diseases.

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