demonstrated that, although characterised by similar anatomical organization, ELS pathogenic cytokine signature is associated with low levels of bcl6 and AID and aberrant apoptosis, unveiling impaired regulation of the B cell cycle, responsible for the survival of autoreactive, poorly selected B cell clones. Accordingly, selective depletion of ELS *in vivo* profoundly impact local and systemic autoimmunity.

REFERENCE

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Disclosure of Interest None declared.

P010

CHARACTERIZATION OF DISTINCT DENDRITIC CELL SUBSETS IN THE CONTEXT OF CHRONIC INFLAMMATION

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Career situation of first and presenting author Assistant.

Introduction Dendritic cells (DCs) are central regulators of the balance between immunity and tolerance, and alteration of the specialized DCs system is a common feature in chronic inflammatory diseases, such as rheumatoid arthritis (RA). In RA, synovial tissues are characterized by aberrant distribution of DCs populations, with altered phenotype. However, an in-depth characterization of the altered phenotype and functions of DCs in RA has been hampered by a lack of specific DCs markers and relevant *in vitro* culture model.

Objectives To perform an in-depth phenotypic characterization of DCs found in RA joints with an extensive panel of monoclonal antibodies specific of DCs, and to establish a relevant *in vitro* culture model to generate DCs resembling to those found in joints.

Methods Flow cytometry was used for analysis of cell surface molecules expressed on DCs found in RA synovial fluid (SF). Staining was performed with a panel of 100 mouse monoclonal antibodies specific of DCs, generated by immunization with different subsets of human DCs. Phenotype of DCs from synovial fluid was then compared to the phenotype of monocytes co-cultured *in vitro* with synoviocytes from RA patients, in presence or not of synovial fluid, or cytokines.

Results In RA SF patients, two main DCs subsets were identified, with distinct surface protein phenotypes. One subset was characterized by markers of plasmacytoid DCs (CD303, CD123), whereas the other subset expressed markers of myeloid/conventional DCs (CD11c, DCIR). This last subset of DCs expressed some markers found on inflammatory DCs, the main inducers of Th17 cells in RA joints. Surprisingly, the two subsets of DCs expressed also surface proteins shared by synoviocytes. Culture of human monocytes with synoviocytes and/or combination of pro-inflammatory cytokines (TNF, M-CSF, IL-4) yielded DCs with a phenotype close to the phenotype of conventional DCs found in RA synovial fluid.

Conclusions We uncovered previously unreported phenotypic heterogeneity of DCs in a chronic inflammatory context, and characterized two main subsets of DCs. The next steps will be

to understand the consequences of this heterogeneity on the pathogenicity of the disease. This will be facilitated by our relevant *in vitro* culture model that allows the generation of DCs, closely resembling those found in joints of patients with RA.

Disclosure of Interest None declared.

P011

THE ROLE OF CELLULAR METABOLISM IN RHEUMATOID AND PSORIATIC ARTHRITIS

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Introduction Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) share common features such as synovial hyperplasia, cartilage degradation and subchondral bone remodelling, however, there are distinct pathologic differences, which aid their diagnosis, and may account for the differential responses to specific treatments. Increased proliferation and angiogenesis transforms the synovium into an aggressive, tumour-like 'pannus' which contributes to disease pathogenesis. Hypoxia, resulting from dysregulated angiogenesis, can cause cells to switch from mitochondrial respiration to anaerobic glycolysis in order to meet the cellular energy demand. The RA synovium is more hyperplastic and invasive than that of PsA, while a more abnormal vasculature is observed in the PsA synovium and correlates with a reduction in tissue pO₂ levels.

Objectives The aim of this study was to compare the metabolic profiles of RA and PsA synovial fibroblast cells (SFC) and to determine whether there is a correlation between dysregulated metabolism, cell function and disease pathogenesis.

Methods The metabolic profiles of RA and PsA SFC were analysed using the XF96 Extracellular Flux Analyzer. Gene expression was determined by quantitative-PCR. SFC migration and invasion were observed by microscopy following wound-scratch and transwell invasion assays.

Results RA SFC displayed increased migratory capacity and invasiveness compared to PsA SFC. Expression of IL-6, IL-8 and the glycolytic markers, GLUT1/3, HK2, PKM1/2, PDK2 and LDHA is higher in RA SFC compared to PsA SFC and is upregulated following TNF- α treatment. PsA SFC displayed higher baseline oxygen consumption rate (OCR), baseline extracellular acidification rate (ECAR) and ECAR:OCR ratio than RA SFC. Treatment with TNF- α increases the ECAR:OCR ratio in both RA and PsA SFC.

Conclusions Consistent with clinical observations, RA SFC have a greater migratory and invasive capacity than PsA SFC. Despite the lower expression of glycolytic markers, PsA SFC display a more glycolytic phenotype than RA SFC, as indicated by a higher ECAR:OCR ratio. Interestingly, however, RA SFC display a higher glycolytic reserve, possibly due to the higher expression of glycolytic markers, which can be called upon in response to increases in cellular ATP demand. Preliminary data suggest a positive correlation between the ECAR:OCR ratio and DAS28 in RA but a negative correlation in PsA. Further investigation is required to determine the precise role of metabolism in specific pathogenic processes.

Disclosure of Interest None declared.