addition, the inflammation marker ESR was negatively correlated with TFH as well as with the differentiated B cell subsets in female patients. Our observations indicates a role of the humoral immune response in AS.

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OP0025

CD209+/CD14+ DENDRITIC CELLS ARE ENRICHED AND ACTIVATED AT THE SITE OF INFLAMMATION AND ARE MODULATED BY JAK/STAT SIGNALLING

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Background: Dendritic cells (DCs) are a heterogeneous population of professional antigen-presenting cells which are at the interface between innate and adaptive immunity. A specific subset of DCs is known to derive from monocyte and has a key role in inflammation and infection.

Objectives: This study aimed to characterize the phenotype and function of a distinct CD209⁺/CD14⁺ DC subset in the periphery and at the site of inflammation in patients with rheumatoid (RA) and psoriatic arthritic (PsA), in addition to examining the effect Tofacitinib and TNF inhibitor on their development.

Methods: Peripheral blood and synovial fluid mononuclear cells (PBMC and SFMC) were isolated by Ficoll density gradient from healthy subject (HC), and patients with RA and PsA. Single cell synovial tissue suspension (ST) from RA and PsA patients were also established using enzymatic/mechanical digestion. PBMC, SFMC and ST were analysed by flow cytometry to identify the CD209⁺/CD14⁺ DC subset, its frequency and the cell surface expression of chemokines receptors (CCR6, CCR7, CXCR3, CXCR4 and CXCR5) and activation markers (CD40 and CD80). In addition, PBMC were stimulated with different TLR (LPS, CPG, R848, Poly I:C) and intracellular staining for IL12, TNF α , IL1 β and IL6 was performed by flow cytometry. Lineage negative cells (CD3/CD19/CD56⁺) were stimulate with GMCSF/IL4 in the presence or absence of the JAK/STAT inhibitor Tofacitinib or the TNF inhibitor Humira, and the CD209⁺/CD14⁺ DC development was evaluated by flow cytometry.

Results: We identified, for the first time, a distinct CD209⁺/CD14⁺ DC population in PBMC of patients with RA and PsA, with similar frequency across the groups. However, when PBMC were stimulated with TLRs, an increase of IL12 and TNF α was observed in RA and PsA PBMC when compared to HC. Interestingly, this distinct DC population was significantly enriched at the site of inflammation, in both SFMC and ST, displaying a more mature phenotype, evident by the observed significant increase in CD40 and CD80 expression. SPICE analysis further identified differential expression and co-expression of chemokine receptors at the periphery of RA and PsA patients, when compared to the HC. Furthermore synovial tissue single cell analysis from RA/PsA demonstrated a unique chemokines receptors profile demonstrating increased single expression and co-expression of CXCR3 and CXCR5 compared to periphery. Finally, we have previously observed that JAK/STAT is involved in monocyte-derived dendritic cells population development (1,2), therefore we performed CD3, CD19 and CD56 depletion of RA/PsA PBMC followed by stimulation with GMCSF/IL4, to spike the Mo-DC population, in the presence of Tofacitinib or Humira. Interestingly, we observed that JAK/STAT inhibition, but not TNF inhibitor, reduced the generation and development of CD209⁺/CD14⁺ DC.

Conclusion: We identify for the first time a distinct monocyte-derived DC population characterized as CD209⁺/CD14⁺ in the periphery of RA and PsA patients. This population was enriched at the site of inflammation and displayed a unique chemokine receptor profile and activation markers, suggesting that these cells are already activated in the periphery of IA patients, and are recruited and further activated in the inflamed joint. In addition, we showed that the CD209⁺/CD14⁺ DC development is regulated by JAK/STAT signalling, but not TNF inhibition.

REFERENCES:

- Marzaioli V, Canavan M, Floudas A, et al. Monocyte-Derived Dendritic Cell Differentiation in Inflammatory Arthritis Is Regulated by the JAK/STAT Axis via NADPH Oxidase Regulation. *Front. Immunol.* 2020;11:1406.
- Marzaioli V, Hurtado-Nedelec M, Pintard C, et al. NOX5 and p22phox are 2 novel regulators of human monocyte differentiation into dendritic cells. *Blood.* 2017;130(15):1734–1745.

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OP0026

IGF1R DEPENDENT CELL INTERACTION AND REGULATION OF AUTOANTIBODY PRODUCTION IN RHEUMATOID ARTHRITIS

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Background: The insulin-like growth factor 1 receptor (IGF1R) signalling mediates numerous developmental processes acting through downstream adaptor molecules IRS1/2, which activate Akt and inhibit the family of forkhead box class O (FoxO). Inhibition of IGF1R signalling alleviates rheumatoid arthritis (RA) (Erlandsson et al., 2017), however, the role of IGF1R signalling in the regulation of immune function is poorly understood.

Objectives: To investigate the link between IGF1R signalling and antigen presentation in experimental arthritis.

Methods: Arthritis was induced by immunising Balb/c mice with methylated bovine serum albumin (mBSA, n=18) and DBA/1 mice with type II collagen (CII, n=18). The mice were treated with a synthetic IGF1R inhibitor NT157 or with short hairpin RNA targeting IGF1R (shIGF1R) from the day prior to immunisation. Controls were treated with cyclodextrine vehicle/ non-targeting (nt)RNA, respectively. Flow cytometry was used for spleen cell phenotype. Antibody levels were measured by ELISA. Immunohistochemistry (IHC) of spleen was performed for assessment of marginal zone (MZ) and location of pS⁶¹²IRS1+ and pS²⁵⁶FoxO1+ cells. IHC images were acquired by fluorescent confocal microscopy, and analysed using ZEN2009 and Cell Profiler software.

Results: The inhibition of IGF1R resulted in an 80% increase in MZ area in NT157-treated mice compared to controls (p=0.0001). This was supported by a significant increase of CD21+ (p=0.034) and CD23+ cell populations (p=0.00059), both among the CD19+ B cells and antigen-presenting MHCII+CD19- cells, implying that IGF1R expression regulates the populations of MZ and follicular cells. Additionally, there was a strong positive correlation between the decrease of IGF1R+ and ICOSL+ population on CD21+ cells (r=0.70, p=0.0071), which retained them in the MZ and prolonged communication with macrophages. Insufficient feedback from ICOSL- B cells limited expression of CXCR5 on CD4 cells. The IHC analysis displayed that, IGF1R inhibition led to abundance of inactive pS⁶¹²IRS1+ and pS²⁵⁶FoxO1+ cells within the MZ, compared with controls (p=0.0002). Alongside the increase of IgM+ B cell population (p=0.0022), we observed significant increase in number of antigen-presenting F4/80+ cells (p=0.043) and MARCO expression (p=0.043) after IGF1R intervention. Finally, the NT157- treated mice displayed a significant pleiotropic increase in IgM autoantibody production, with anti-CCP IgM (p=0.027), RF-IgM (p=0.0085), anti-DNA IgM (p=0.066) and in total IgM (p=0.027) levels, which correlated positively with pS²⁵⁶FoxO1+ cells (r=0.51, p=0.03). Levels of IgG were not changed.

Conclusion: We show that IGF1R signalling is important for immune cell communication after antigen challenge. IGF1R controls ICOSL dependent trafficking of B cells through the MZ and facilitates interaction with T cells. Retention of B cells in the MZ tips the balance from T cell to macrophage-dependent processes, which permits the formation of autoantibody producing B cells.

REFERENCES:

- Erlandsson, M., et al., 2017. IGF-1R signalling contributes to IL-6 production and T cell dependent inflammation in rheumatoid arthritis. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, 1863(9), pp.2158-2170.

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OP0027

AS-RELATED TCR BETA CLONOTYPES ARE PRESENT IN DIFFERENT INFLAMED TISSUES OF PATIENTS WITH SPONDYLOARTHROPATHIES

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