Results: Myeloid DCs are scarce in control non-inflammatory OA synovial tissues and their number increased substantially in PsA and RA tissues. Phenotyping data revealed that all myeloid DC subsets can be present in inflamed RA and PsA synovium. However, CD1c⁺ DC populations (DC2/DC3) were the most abundant in RA synovial tissues and the gene expression analysis of CD1c⁺ sorted from RA synovial biopsies showed an increase in the expression of epigenetic regulator of inflammatory response miR-155 and IL-6, TNF and IL-23 as compared to circulating cells.

Conclusions: CD1c⁺DCs from RA synovial tissues had epigenetically regulated activated phenotype (miR-155 and miR-34a²) that through the production of cytokines could maintain tissue activation of autoreactive Th1 and Th17 cells and contribute to inflammation.

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SAT0004

INTRARTICULAR INJECTION OF ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS REDUCE EXPERIMENTAL OA PATHOLOGY VIA IL-1B-MEDIATED REALLOCATION AND ENHANCED PHAGOCYTOSIS OF POLYMORPHONUCLEAR LEUCOCYTES

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Background: Injection of adipose-derived mesenchymal stromal cells (ASCs) into knee joints after induction of experimental inflammatory osteoarthritis (CiOA) reduces development of joint pathology.¹ This protection is only achieved when ASCs are applied in early CiOA, which is characterised by synovitis and high levels of S100A8/A9 and IL-1 β , suggesting that inflammation boosts the protective effect of ASCs.²

Objectives: To examine the role of synovitis in ASC-mediated amelioration of CiOA pathology.

Methods: CiOA was induced by intra-articular collagenase injection. Knee joint sections were stained with haematoxylin/eosin and immunolocalization of polymorphonuclear leucocytes (PMNs) and ASCs was performed using antibodies for NIMP-R14 and CD271, respectively. Chemokine expression induced by IL-1 β or S100A8/A9 was assessed with qPCR and Luminex. Migration of PMNs through transwell membranes towards ASC-conditioned medium (CM) was examined using flow cytometry. ASC-PMN co-cultures were analysed microscopically and with Luminex. Phagocytic capacity of PMNs was measured with labelled zymosan particles.

Results: Intra-articular injection of saline in knee joints of day 7 CiOA induced a flare already after 6 hours, characterised by particularly PMNs scattered throughout the synovium. Although ASC injection resulted in comparable numbers of PMNs, these cells however, were clustered around ASCs. IL-1 β -stimulation of ASCs *in vitro* strongly increased expression of PMN-attracting chemokines KC, CXCL5, and CXCL7, whereas S100A8/A9 did not. Migration of PMNs towards CM of IL-1 β -stimulated ASCs (IL-1 β -CM) was significantly enhanced (2.9-fold increase) when compared to CM of non-stimulated ASCs (NS-CM). After 6 hours co-culturing PMNs with IL-1 β -stimulated ASCs, the number of clustered PMNs per ASC was significantly increased. Interestingly, association of PMNs with ASCs significantly diminished the release of KC protein by ASCs (69% lower after 24 hour), and also strongly reduced the release of S100A8/A9 protein by the PMNs. Moreover, phagocytic capacity of PMNs was strongly enhanced after priming with CM of IL-1 β -stimulated ASCs.

Conclusions: Local application of ASCs in inflamed CiOA knee joints results in attraction and clustering of PMNs with ASCs in the synovium, which is likely mediated by IL-1 β -induced up-regulation of chemokine release by ASCs. This results in lowered S100A8/A9 levels and enhanced phagocytic capacity of PMNs, enabling the clearance of debris to attenuate synovitis and promote tissue repair.

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SAT0005

INTERLEUKIN-33 AMELIORATES MURINE LUPUS VIA INDUCTION OF REGULATORY T CELLS AND M2 MACROPHAGE POLARISATION

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Background: The levels of IL-33, a Th2 promoting cytokine, and the soluble form of its receptor ST2 were reported to be elevated in serum of patients with active systemic lupus erythematosus (SLE), suggesting a role of the IL-33/ST2 axis in the pathogenesis of SLE.

Objectives: This study aims to examine the effect of IL-33 in disease severity of murine lupus.

Methods: IL-33 was injected intraperitoneally 3 times per week to pre-diseased MRL/lpr mice aged 12 weeks for 6 weeks. Control group was given 1% BSA injection. Urine protein was monitored weekly by albustix and protein assay. Immunophenotyping of splenocytes was examined by flow cytometry. Splenic CD11b+monocytic cells were isolated by microbeads for mRNA examination.

Results: IL-33-treated mice (n=9) developed significantly less proteinuria compared to BSA-treated group (n=9). Kidney histology of the IL-33-treated group showed remarkably less mesangial deposit, diffuse proliferative glomerular changes and crescents, and had significantly lower renal composite score compared to controls (median 2.0 vs 9.9, p<0.001). Kidneys of these mice expressed lower mRNA levels of TNF- α (32.1 $\pm$ 14.7 vs 77.0 $\pm$ 27.8, p<0.001), IL-6 (median 0.6 vs 4.7, p=0.003), IL-1 β (31.1 $\pm$ 10.1 vs 77.8 $\pm$ 24.6, p<0.001) and iNOS (p=0.006). Immunophenotyping of splenocytes showed significantly increased CD4+CD25+regulatory T (Treg) cells (4.0 $\pm$ 1.2% vs 2.2 $\pm$ 0.2%, p<0.001) that expressed remarkably higher Foxp3 (76.0 $\pm$ 5.0% vs 59.3 $\pm$ 12.6%, p=0.002). Splenic extracts showed predominant Gata3 (0.37 $\pm$ 0.20 vs 0.12 $\pm$ 0.09, p=0.01) and Foxp3 (0.42 $\pm$ 0.16 vs 0.17 $\pm$ 0.11, p=0.002) mRNA in IL-33-treated mice. These Treg cells expressed high cell surface ST2 (8.9 $\pm$ 2.7% vs 4.5 $\pm$ 2.0%, p=0.008). There was significant expansion of splenic CD11b+population in IL-33-treated mice (17.8 $\pm$ 10.5 vs 8.8 $\pm$ 3.0, p=0.01) that expressed significantly higher CD206 (5.2 $\pm$ 0.9% vs 2.9 $\pm$ 0.9%, p=0.002). Isolated splenic CD11b+cells expressed significantly higher mRNA of Arg1, FIZZ1 and Ym-1 and IL-10 (all p=0.01) with reduced expression of iNOS (p=0.02). Kidney extracts of IL-33 treated mice also had elevated mRNA levels of M2 markers including Arg1 (median 199.8 vs 36.1, p=0.004) and FIZZ1 (median 25.0 vs 2.7, p<0.001) and reduced MCP-1 (12.7 $\pm$ 6.5 vs 35.1 $\pm$ 12.0, p<0.001). There was also significantly higher levels of mRNA of Foxp3 (median 43.0 vs 20.8, p=0.006) and Gata 3 (1.7 $\pm$ 0.5 vs 0.9 $\pm$ 0.5, p=0.008) but lower Rorc (2.6 $\pm$ 1.0 vs 3.8 $\pm$ 0.8, p=0.008) and Tbx21 (12.6 $\pm$ 6.0 vs 29.6 $\pm$ 13.7, p=0.003) in the kidneys.

Conclusions: Exogenous IL-33 led to significantly less proteinuria and renal inflammation. These mice had significantly higher splenic Treg cells with prominent Foxp3 expression. Isolated CD11b+cells from spleen and kidney extracts demonstrated mRNA levels of M2 macrophage polarisation.

Disclosure of Interest: None declared

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SAT0006

P2X7 RECEPTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). EXPLORING A NOVEL PATHOGENETIC PATHWAY IN LUPUS RELATED SEROSITIS

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Background: Recent studies have focused attention on the involvement of innate immunity and in particular on the activation of NLRP3 inflammasome by purinergic signalling mediated by P2 $\times$ 7 receptor (P2 $\times$ 7R), in SLE pathogenesis.¹ Serositis are typical SLE manifestations often associated with increased inflammatory indices and promptly responding to colchicine whose action could be mediated by its effect on microtubules during P2 $\times$ 7R assembly.

Objectives: To explore the role of innate immune system in SLE evaluating expression and activity of P2 $\times$ 7R and NLRP3, comparing patients with positive and negative history of serositis with healthy control subjects (HC).