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/DC3s) 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 to compare circulating cells.

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

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Disclosure of Interest: None declared
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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 albumin and protein assay. Immuno-phenotyping of splenocytes was examined by flow cytometry. Splenic CD11b+ monocytes 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). Kidney extracts of these mice expressed lower mRNA levels of TNF (p=0.03±1.7 vs 77.2±27.3, p<0.001), IL-6 (median 0.6 vs 4.7, p=0.003), IL-1 (31.1±10.1 vs 77.8±24.6, p<0.001) and INOS (p=0.006). Immuno-phenotyping of splenocytes showed significantly increased CD4+CD25+regulatory T (Treg) cells (4.0%±1.2% vs 2.2%±0.2%, p<0.001) that expressed remarkably higher Foxp3 (76.0%±5.5% vs 59.3±12.6%, p=0.002). Splenic extracts showed predominant Gata3 (0.37±0.20 vs 0.12±0.09, p=0.01) and Foxp3 (0.42±0.16 vs 0.17±0.11, p=0.002) mRNA in IL-33-treated mice. These Treg cells expressed high cell surface ST2 (8.9%±2.7% vs 4.5±2.0%, p=0.008). There was significant expansion of splenic CD11b+ population in IL-33-treated mice (17.8±10.5 vs 8.8±3.0, p=0.01) that expressed significantly higher CD206 (5.2%±0.9% vs 2.9%±0.9%, p=0.002). Isolated splenic CD11b+ cells expressed significantly higher mRNA of Arg1, FIZZI 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 FIZZI (median 25.0 vs 2.7, p<0.001) and reduced MCP-1 (12.7±6.5 vs 35.1±12.0, p=0.010). There was also significantly higher levels of mRNA of F003P (median 43.0 vs 20.8, p=0.006) and Gata 3 (1.7±0.5 vs 0.9±0.5, p=0.008) but lower Rorc (2.6±1.0 vs 3.8±0.8, p=0.008) and Th22 (12.6±5.0 vs 25.6±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 markedly reduced mRNA levels of M2 macrophage polarisation.

Disclosure of Interest: None declared

SAT0006 P2X7 RECEPTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), EXPLORING A NOVEL PATHOGENETIC PATHWAY IN LUPUS RELATED SEROSEITIS

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Background: Recent studies have focused attention on the involvement of innate immunity in lupus and in particular on the activation of NLRP3 inflammasome by purinergic signalling mediated by P2X7 receptor (P2X7R). In SLE pathogene- sis, 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 P2X7R assembly.

Objectives: To explore the role of innate immune system in SLE evaluating expression and activity of P2X7R and NLRP3, comparing patients with positive and negative history of serositis with healthy control subjects (HC).

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, DC1c+ DC populations (DC2/DC3s) were the most abundant in RA synovial tissues and the gene expression analysis of DC1c+ 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 to compare circulating cells.

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