Background/purpose Dendritic cells (DC) are key cells in the pathogenesis of autoimmune diseases by potently activating T-cells. Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are characterised by an IFN signature, caused by elevated levels of IFNα. Plasmacytoid DC (pDC) are held responsible for the increased levels of IFNα in SLE and APS. The molecular mechanisms underlying the increased activation of pDC in SLE and APS are unknown. Using RNA sequencing (RNAseq) and further in vitro validation experiments on plasmacytoid and myeloid DC (mDC) obtained from patients with SLE and APS we assessed the causes and consequences of increased type I IFN signalling on the dysregulation of both pDC and mDC in patients with SLE and APS.

Methods RNAseq was performed on pDC and mDC isolated from peripheral blood of patients with SLE, SLE +APS and primary APS (PAPS) and healthy controls (n=54). Weighted gene correlation network analysis (WGCNA) was used to identify pDC- and mDC-specific gene modules and to stratify patients into those with (IFN-high) or without (IFN-low) an IFN signature. The response of pDC and mDC to IFN-high patients in pDC. In contrast, genes involved in upregulation of co-stimulatory molecules. Furthermore, in SLE/APS the dysregulation of both pDC and mDC were significantly higher in SLE compared to HC (17.0 pg/ml vs 10.2 pg/ml; p=0.001). In vitro, miR-182 could be induced by IL-7, and specific inhibition of miR-182 inhibited T cell proliferation and survival.

Conclusion Our data suggest that enhanced IL7R/STAT5 signalling mediates the induction of miR 182 expression, which promotes the proliferation of conventional Foxp3- T cells SLE. Collectively, our data provide new insights in the pathophysiology of T cell hyperactivity in SLE and identifies miR-182 as a candidate target for future therapeutic approaches.

Background of ACR and were randomly collected in clinical remission state (SLEDAI 1.1±1.9).

Results By comparison of B cell subsets between SLE and HC, CD38 was dominantly expressed by SLE patients (SLE 74.2%±12.9% vs HC 64.2%±12.2%; p(MWU)=0.018). Furthermore, SLE-patients showed an increase in CD19 +IgD CD27 +CD38 high plasmablasts (SLE 2.1%±3.4% vs HC 0.4%±0.4%; p(MWU)<0.001). Moreover, SLE-plasmablasts showed decreased CD73 expression as compared to HC (SLE 2.1%±1.9% vs HC 3.5%±2.2%; p(MWU)=0.034). SLE-B cells revealed a trend towards an augmented CD38highCD138 +plasmacell fraction (SLE 0.40%±0.5% vs HC 0.08%±0.07%; p=0.07), without any difference in CD73 expression. On the other hand, exhausted-memory B cell fraction (CD19 +IgD CD27-CD21-CD138-), showed an increased CD73 expression in SLE (SLE 13.7%±9.2% vs HC 6.2%±5.4%; p=0.004).

Conclusion Our study confirms CD38 +plasmablasts as being increased in peripheral blood from SLE patients as compared to HC. Furthermore, the data reveal a deficiency for CD73 on SLE plasmablasts, which suggests a decreased regulatory capacity of SLE plasmablasts as compared to HC, supporting the notion of a reduced regulatory B cell pool in SLE. On the other hand, the enlarged CD73 +exhausted memory pool in SLE could point to an accelerated flow of CD73 +regulatory B cells into an exhausted B cell fraction. These findings support the hypothesis of a persistent regulatory B cell defect even in a state of SLE remission.

Abstracts