Systemic lupus erythematous (SLE) is a prototypical autoimmune disease resulting in multi-organ damage and a high rate of morbidity. Onset of SLE is characterised by dysregulated activation of T and B lymphocytes and the production of autoantibodies directed against nuclear components. The autoantibodies generated during the onset of SLE often recognise components released by neutrophils during NETosis, a type of cell death defined by the generation of neutrophil extracellular traps (NETs). The endonuclease DNase I has been shown to be involved in the clearance of NET components. The sera of SLE patients contain inhibitors of DNase I and/or anti-NET antibodies that block the ability of DNase I to degrade NETs. Thus, whilst NETs are important for clearing infection they must be tightly regulated and degraded to prevent the onset of autoimmunity.

In this study we monitored the production of autoantibodies in the serum of wild type and DNase I deficient mice from the age of 2 to 12 months, along with proteinuria levels and the development of glomerulonephritis. We show that DNase I deficient mice develop a SLE-like phenotype with elevated auto-antibody production and kidney damage by 12 months. This model also demonstrates the female bias in SLE in remission in comparison to normal donors. The aim was to follow up persistence of this phenomenon. pDC and mDC produced BAFF and expressed chemokine receptors.

**Conclusion** pDC and mDC are differentially affected by IFNα in SLE and APS. IFNα primes pDC for enhanced IFNα production which potentiates T-cell activation by mDC, thereby sustaining the IFN signature in SLE and APS.
CIRCULATING ANGIOGENIC T-CELLS ARE REDUCED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH HIGH DISEASE ACTIVITY AND WITHOUT KNOWN CARDIOVASCULAR RISK FACTORS

1S Piantoni, 1C Cavazzana, 1M Fredi, 2M Taraborrelli, 1F Franceschini, 1A Tincani, 1P Airo.
1Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Italy; 2Internal Medicine Unit, Mellino Mellini Hospital, Chiari (Brescia), Chiari, Italy

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Background Recent evidences underlined the central role of T-cells in the pathogenesis of Systemic Lupus Erythematosus (SLE) and in its cardiovascular complications.1 CD3 +CD31 +CXCR4 +angiogenic T-cells (Tang) have been identified as a T-cell subtype involved in the repair of damaged endothelium cooperating with endothelial progenitor cells.2 Tang were described as selectively expanded in the circulation of systemic sclerosis patients displaying peripheral vascular complications, as a reaction to an inefficient angiogenesis.3 Not much information is available on Tang in a SLE patients: in a recent study the percentage of circulating CD8 +Tang, but not CD4 +Tang, was higher in SLE than in healthy controls.4 Study was aimed at investigating this subset in patients with systemic lupus erythematosus especially in patients with lupus nephritis. Recently, a separate subset has been discovered characterised by expression of Granzyme B. The aim of this study is to investigate this subset in patients with systemic lupus erythematosus (SLEDAI).

Methods Isolated peripheral blood mononuclear cells of patients with systemic lupus erythematosus (n=30) and healthy controls (n=21) were in vitro stimulated with CPG, IgG +IgM and IL-21. Patients were sub-grouped in patients with and without biopsy proven lupus nephritis. CD19 +B cells were analysed for intracellular Granzyme B expression by flow cytometry. Patients disease activity was assessed by systemic lupus erythematosus disease activity index (SLEDAI).

Results The strongest stimulus for Granzyme B secretion of CD19 +B cells was IgG +IgM in presence of IL-21. Patients with systemic lupus erythematosus had a significant decreased percentage of Granzyme B +CD19 +B cells. This could be shown in particular for patients with active disease and with lupus nephritis.

Conclusions These data demonstrate that CD19 +B cells of patients with systemic lupus erythematosus are impaired to produce Granzyme B. This may contribute to an imbalanced B-cell regulation towards effector B-cells which might promote the development of lupus nephritis.

REFERENCES