APS, pDC and mDC produced BAFF and expressed chemo-
kine receptors.

**Conclusion** pDC and mDC are differentially affected by IFN\(\alpha\) in SLE and APS. IFN\(\alpha\) primes pDC for enhanced IFN\(\alpha\) pro-
duction which potentiates T-cell activation by mDC, thereby
sustaining the IFN signature in SLE and APS.

**PS5:92** CLARIFICATION OF THE ROLE OF DNASE 1 ON THE
ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A
MURINE MODEL

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10.1136/lupus-2018-abstract.137

Systemic lupus erythematosus (SLE) is a prototypical autoim-
mune disease resulting in multi-organ damage and a high rate of
moribundity. Onset of SLE is characterised by dysregulated
activation of T and B lymphocytes and the production of
autoantibodies directed against nuclear components. The auto-
antibodies 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 DNase1 has been shown to
be involved in the clearance of NET components. The sera of
SLE patients contain inhibitors of DNase 1 and/or anti-NET
antibodies that block the ability of DNase1 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 auto-antibod-
ies in the serum of wild type and DNase 1-deficient mice from
the age of 2 to 12 months, along with proteinuria levels and the
development of glomerulonephritis. We show that
DNase 1-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
as the female DNase 1-deficient mice had the highest level of
kidney damage. As DNase 1 activity, B cells and aberrant
NETosis are central to progression of SLE understanding their
mechanisms of action are of great therapeutic interest.

**PS5:94** CHARACTERISATION OF SLE B CELLS FROM PATIENTS
IN REMISSION – PERSISTENT IL-10 SECRETORY DEFECT

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10.1136/lupus-2018-abstract.139

Background SLE is an autoimmune disorder characterised by
polyclonal Bcell activation, the production of anti-double
stranded (ds) DNA autoantibodies and cytokines. Molecular
and clinical studies regarding SLE often address clinically
active patients and not patients in remission. This study reports
on immunoglobulin, anti-dsDNA-aab and IL-10 secretory
capacity of cultures of CD19 +lymphocytes from SLE patients
in remission in comparison to normal donors. The aim was to
evaluate whether endogenous factors (BAFF, CD40, IL4),
exogenous factors (CpG-ODN-motifs, SAC) or their combina-
tions differentially influence immunoglobulin, cytokine and
anti-dsDNA-aab production in not active SLE patients vs
healthy controls.

**Methods** Blood samples were obtained from a group of 13 SLE
patients attending clinics at the rheumatology unit at the Heinrich-
Heine University hospital in Düsseldorf and from 5 healthy controls (HC). All patients were randomly collected in clinical remission state (SLEDAI 1,±1,8). The medication consisted of prednisolone (5/13 patients), mycophenolate mofetil (3/13 patients), azathioprine (1/13 patients), hydroxychloroquine (8/13 patients) or was without immunosuppression.

After 6 days of cell culture levels of IgG, IgM, dsDNA antibodies and interleukin-10 (IL-10) were determined in the supernatants by ELISA. The effect of the stimuli alone or in combination on IgG, IgM, anti-dsDNA-aab, and IL-10 production was analysed.

Results Peripheral B cells from SLE patients in remission or control subjects did not show any difference in IgG, IgM, and anti-dsDNA-aabs to all aforementioned stimuli. The addition of CpG and SAC to cell cultures showed a stimulatory effect on immunoglobulin, cytokine and anti-dsDNA-aab production in SLE B cells and healthy controls alike. The amount of anti-dsDNA IgG-type autoantibodies produced by peripheral B cells was negligible. However, B cells from SLE patients showed diminished capacity to produce IL-10 as compared to B cells from healthy donors (SLE Estimate -40.17, Std.error 17.21, p<0.01). The strongest stimulus for Granzyme B secretion of B cells from patients with systemic lupus erythematosus was higher in SLE than in healthy controls.4 These data demonstrate that CD19+B cells of patients with lupus nephritis. Recently, a separate subset has been discovered with systemic lupus erythematosus especially in patients with lupus nephritis. The aim of this study is to investigate this subset in patients with systemic lupus erythematosus disease activity index (SLEDAI).

References

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.3 However, in this study SLE patients with hypertension, dyslipidemia or smoking habit, factors which may influence Tang counts, were not excluded.

The aim of this study was to characterise Tang in a cohort of patients with SLE without known cardiovascular risk factors.

Methods Twenty female SLE patients with a recent disease onset (<5 years) and without traditional cardiovascular risk factors or previous events (age: median value = 43 [25th-75th percentile=27–54] years) and 18 healthy controls (age: 40 [32–54] years) were enrolled.

Phenotypic analysis of peripheral Tang lymphocytes was made by flow-cytometry.

Disease activity was evaluated by SLEDAI-2K score.

Results SLE patients were divided in two groups according with disease activity. Patients with SLEDAI-2K equal or higher than 6 were defined as patients with high disease activity (n:5). They had a lower percentage of circulating Tang in comparison with healthy controls (10 [8–15] vs 16 [14–23]% of CD3 +T cells, p=0.04). The result was confirmed in absolute number (83 [60-103] vs 242 [165-328] cell/microliter, p=0.04). SLE patients with low disease activity had levels of Tang which were intermediate between, and not significantly different from, healthy controls and patients with high disease activity.

Conclusions Tang were reduced in our patients with active SLE, and no known cardiovascular risk factors, suggesting that this reduction was directly explained by disease activity.

Abstracts

CIRCULATING ANGIOGENIC T-CELLS ARE REDUCED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH HIGH DISEASE ACTIVITY AND WITHOUT KNOWN CARDIOVASCULAR RISK FACTORS

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10.1136/lupus-2018-abstract.140

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.3 However, in this study SLE patients with hypertension, dyslipidemia or smoking habit, factors which may influence Tang counts, were not excluded.

The aim of this study was to characterise Tang in a cohort of patients with SLE without known cardiovascular risk factors.

Methods Twenty female SLE patients with a recent disease onset (<5 years) and without traditional cardiovascular risk factors or previous events (age: median value = 43 [25th-75th percentile=27–54] years) and 18 healthy controls (age: 40 [32–54] years) were enrolled.

Phenotypic analysis of peripheral Tang lymphocytes was made by flow-cytometry.

Disease activity was evaluated by SLEDAI-2K score.

Results SLE patients were divided in two groups according with disease activity. Patients with SLEDAI-2K equal or higher than 6 were defined as patients with high disease activity (n:5). They had a lower percentage of circulating Tang in comparison with healthy controls (10 [8–15] vs 16 [14–23]% of CD3 +T cells, p=0.04). The result was confirmed in absolute number (83 [60-103] vs 242 [165-328] cell/microliter, p=0.04). SLE patients with low disease activity had levels of Tang which were intermediate between, and not significantly different from, healthy controls and patients with high disease activity.

Conclusions Tang were reduced in our patients with active SLE, and no known cardiovascular risk factors, suggesting that this reduction was directly explained by disease activity.

REFERENCES

Objective B-cells play a crucial role in the pathogenesis of 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 especially in patients with lupus nephritis.

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.