PS5:97 ROLE OF CD107A+ (LAMP-1) CYTOTOXIC CD8+ T-CELLS IN PATIENTS WITH SLE

[1]A Wiechmann, [1]B Wilde, [1]A Kribben, [2]O Witzke, [2]S Dolff. [1]*Department of Nephrology, University Hospital Essen, Germany*; [2]*Department of Infectious Diseases, University Hospital Essen, Germany*

10.1136/lupus-2018-abstract.142

Objectives Cytotoxic T-cells are a thought to play a pivotal role in the pathogenesis of systemic lupus erythematosus (SLE) in particular in lupus nephritis. The aim of this study was to investigate the activation marker CD314 (NKG2D) and CD107a (LAMP-1) on cytotoxic CD8 +T cells in patients with systemic lupus erythematosus.
Methods Peripheral blood of patients with systemic lupus erythematosus (n=30) and healthy controls (n=21) was stained with anti-CD8 (PB), -CD3 (Chrom Orange), -CD45RO (FITC), -CD197 (PE), -CD314 (APC), -CD107a (APC) antibodies and analysed by flow cytometry. Kidney biopsies of lupus nephritis patients were investigated by immunohistochemistry and immunofluorescence for the presence of CD8 +C107a+cells. Patients disease activity was assessed by systemic lupus erythematosus disease activity index (SLEDAI).
Results The percentages of CD314 +on CD8+T cells were not different between SLE-patients and healthy controls. The percentages of CD107a+on CD8+T cells were significantly decreased in SLE-patients as compared to healthy controls (40.2%±18.5% vs 47.9±15.0%, p=0.02). This was even more significant in SLE-patients with inactive disease. The evaluation of lupus nephritis biopsies showed a significant number of CD107a+CD8+T cells mainly located in the peritubular infiltrates.
Conclusions These results demonstrate that CD8 +T cells of patients with systemic lupus erythematosus have an altered activation status which seems to be associated with disease activity. The proof of intrarenal CD107a+CD8+suggests a role in the pathogenesis of lupus nephritis.

PS5:98 TCR ZETA DIM LYMPHOCYTES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

[1]M Szmyrka, [2]L Ciszak, [2]A Szteblich, [3]M Weglarz, [2]A Kosmaczewska. [1]*Wroclaw Medical University, Dept. of Rheumatology and Internal Diseases, Wroclaw, Poland*; [2]*Ludwik Hirszfeld Institute of Immunology and Experimental Medicine, Dept. of Experimental Therapy, Wroclaw, Poland*; [3]*University of Wroclaw, Dept. of Biotechnology, Wroclaw, Poland*

10.1136/lupus-2018-abstract.143

T lymphocytes with low or absent expression of TCRzeta chain (TCR zeta -/dim cells) are supposed to have pathogenic effect in the developement of autoagression and chronic inflammation. Systemic lupus erythematosus (SLE) is a model of chronic inflammatory disease with autoimmune background.

In vitro studies have shown, that microenvironement rich in proinflammatory cytokines, such as TNF-alfa and IL-6, especially promotes the impairment of TCR zeta chain expression, what leads to the increase of the percentage of T cells with defects of the synthesis of that molecule.
Objective The aim of this study was to define the size of the population of autoreactive TCR zeta -/dim lymphocytes in the blood of patients with SLE and the functional characteristics of TCR zeta-/dim and TCR zeta bright cells based on the assessment of their capacity to synthetize certain cytokines (IFN-gamma and IL-2) and to compare it with healthy controls.
Results Our study showed decreased percentage of CD4 +and CD8+lymphocytes with TCR zeta chain expression in patients with SLE. The significantly diminished TCRzeta chain expression in lymphocytes of patients with SLE which in addition was correlated with longer disease duration, renal involvement and higher level of serum anti-dsDNA antibodies confirms former studies indicating not only the association of this defect with disease developement, but also with more active clinical course.

The *in vitro* stimulation of T lymphocytes in SLE patients lead to overproduction of IFN-gamma especially in the population of autoreactive TCR zeta -/dim lymphocytes.

On the other hand, T lymphocytes of SLE patients have lower capacity of the synthesis of IL-2, which is strongly correlated with TCR zeta chain expression and may be observed even in patients with very low clinical disease activity.
Conclusion SLE is characterised by the expanssion of TCR zeta -/dim lymphocytes in peripheral blood, which are regarded as autoreactive cells, and is correlated with clinical course of SLE. The decreased expression of TCR zeta may be due to the presence of exogenous inhibiting factor in blood of SLE patients. Higher synthesis of INF-gamma and lower of IL-2 may contribute to chronic inflammation and autoimmune proces in SLE.

PS5:99 EXAMINING THE MODULATORY EFFECTS OF ANTI-SERINE PROTEASE ANTIBODIES UPON FACTOR XA, THROMBIN AND COMPLEMENT INTERACTIONS

[1]T McDonnell, [1]C Wincup, [1]V Ripoll, [2]C Gerveshi, [1]A Rahman, [1]I Mackie, [3]M Botto, [1]I Giles. [1]*University College London, UK*; [2]*Drexel University, Philadelphia, USA*; [3]*Imperial College London, UK*

10.1136/lupus-2018-abstract.144

Purpose Serine protease (SP) enzymes play a critical role in both the coagulation and complement cascades. Anti-SP antibodies are found in approximately 40% of patients systemic lupus erythematosus (SLE) and antiphospholipid Syndrome (APS). Complement activation is important in SLE and APS. However, little is known about the effects of anti-SP antibodies on complement activation in these diseases. We sought to investigate whether affinity-purified antibodies to the SP Factor(F)Xa and Thrombin (Thr) alter the effects of these SP on complement cleavage in the presence or absence of the physiological inhibitor anti-thrombin (AT).
Methods Serum was obtained by informed consent from patients with SLE (n=10) and/or APS (n=2) under long-term follow-up at University College London Hospital. A novel method was developed to affinity purify anti-FXa and anti-Thr IgG separately. We incubated FXa (2 μM) and Thr (2.7 μM) separately with complement component C3 to determine baseline C3 cleavage. We then repeated the experiment in the presence of AT3, the appropriate anti-SP (anti-FXa or anti-Thr) or both. Finally we reviewed medical records of 40 patients with SLE to determine whether low C3 was associated with seropositivity for anti-FXa and/or anti-Thr in these patients.
Results Both FXa and Thr cleaved C3 into C3a/C3 b. This was inhibited by AT, though both cleavage and inhibition by AT were stronger for Thr than FXa. Conversely anti-SP antibodies enhanced C3 cleavage by SP. Anti-FXa IgG (n=3) increased FXa-mediated cleavage of C3 by 1.3-fold. Anti-Thr IgG (n=8) increased Thr-mediated C3 cleavage by 1.8-fold. AT mediated inhibition was prevented by addition of anti-FXa