

**Background and objectives** Loss of tolerance towards nuclear antigens such as SmD1, RNP70, Histone, Ro, and La due to defective disposal of biological waste is characteristic of SLE. The question whether CD4 +T cells reactive to the aforementioned autoantigens are also implicated in SLE remains unclear. To study the role of autoreactive CD4 +T cells in SLE, we determined their frequency in healthy and diseased state, investigated their antigen specificity, characterised their cytokine production, interrogated their localization in the tissue, and analysed their homeostatic balance with autoreactive regulatory T cells (Treg).

**Materials and methods** We employed: T cell library to detect peripheral nuclear autoantigen-reactive CD4 +T cells, antigen-reactive T cell-enrichment to interrogate their cytokine production, generation of T cell clones and T cell lines to validate their specificity, TCR-beta analysis to predict their clonal occurrence in blood and urine, urinary T cell library to detect and enumerate their frequencies in urine, CFSE-labelled urinary cells to detect and enumerate their frequencies in urine, and enrichment of CD137 +FoxP3+cells to investigate nuclear antigen-reactive Treg.

**Results** The frequency of autoreactive CD4 +T cells is greater in active SLE patients when compared with inactive SLE patients and healthy individuals, and it correlates with disease activity. Single-cell clones of autoreactive CD4 +T cells confirmed their antigen specificity. Autoreactive CD4 +T cells produced pro-inflammatory cytokines such as IFN-gamma, IL-17, and IL-10, where the production of IFN-gamma correlates with disease activity. The accumulation of these cells was detected in urine of active SLE patients with lupus nephritis when compared with their number in the periphery. The ratio of autoreactive effector T cells against autoreactive Treg is higher in active SLE patients when compared with inactive SLE patients and healthy individuals, and it correlates with disease activity.

**Conclusions** Our data demonstrate that higher frequency of autoreactive CD4 +T cells in the periphery could contribute to disease progression of SLE. Accumulation of these cells in urine suggested their possible role in mediating local tissue inflammation. Homeostatic imbalance between autoreactive effector T cells and Treg indicated an insufficient regulatory mechanism to control autoimmunity at antigen-specific level.

**PS5:102 THE EXPRESSION OF BTLA ON CMV-SPECIFIC T-CELLS IS DECREASED IN CMV IGG+ PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Introduction** Cytomegalovirus (CMV) infection is an uncommon but severe infection in patients with systemic lupus erythematosus (SLE) due to immunosuppressive therapy. Standard prophylaxis with antiviral agents or pre-emptive strategies to monitor viral load are not standard of care. The aim of the present study was to investigate the expression of coinhibitory molecules PD-1 and BTLA-4 on CMV specific T-cells in SLE-patients.

**Methods** Sixteen SLE-patients and eight healthy controls were enrolled. Twelve SLE patients were CMV IgG+, four were CMV IgG-. Peripheral blood was sampled and stimulated with CMV lysate, SEB or control serum in presence of anti-CD28/CD49d. After six hours of stimulation, CD154 expression was determined by flow cytometry on CD3 +T cells. The coinhibitory molecules PD-1 and BTLA were determined on activated CD154 +CD3+T cells. Symptomatic CMV infection was defined as CMV syndrome or tissue invasive disease. Asymptomatic CMV infection was defined as detectable CMV replication in peripheral blood and absence of signs indicating CMV syndrome/tissue invasive disease.

**Results** PD-1 and BTLA-4 expression was not significantly different on CMV-specific CD154 +CD3+T cells in SLE-patients as compared to healthy controls. An analysis according to the CMV serostatus revealed a tendency to a decreased proportion of PD-1 +CD154+CD3+T cells in CMV IgG negative patients as compared to CMV IgG positive (24.9%±30.0% vs 35.5±11.5%, p=0.3). The BTLA-4 expression was significantly decreased on CD154 +CD3+T cells in CMV IgG negative patients as compared to CMV IgG positive (70.3%±31.7% vs 95.0±4.3%, p=0.01).

**Conclusion** SLE-patients show a significant decreased expression of BTLA on CMV-specific T-cells. The coinhibitors PD-1 and BTLA usually promote T-cell suppression. Thus a decrease may prone to severe symptomatic infections.

**PS5:103 COSTIMULATORY MAKER ON CYTOTOXIC CD8+ T-CELLS IN PATIENTS WITH SLE**

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**Background** Systemic lupus erythematosus (SLE) is an autoimmune disease where T-cell dependent B-cell activation plays a crucial role. Costimulatory marker promote and inhibit immune responses after ligation. Here we analysed the marker BTLA (CD272), PD-1 (CD279), HLA-DR and HVEM on peripheral cytotoxic T-cells.

**Patients and methods** 30 SLE-patients fulfilling the American College of Rheumatology (ACR) criteria für SLE and 14 healthy controls (HC) were enrolled. Whole blood staining was performed and samples were analysed by multi-colour flow cytometry. Disease activity was assessed by SLEDAI. Renal involvement was defined as biopsy proven lupus nephritis.

**Results** The expression of the costimulatory marker PD-1 is significantly increased on CD8 +T cells in SLE patients as compared to with healthy controls (31.3%±26.7% vs 15.63%±12.22%). We could not found a significant difference in the expression levels of the BTLA receptor on CD8 +T cells (72,24%±15.33 vs 72.66%±9,4%) in SLE patients as compared to with healthy controls. Also HLA-DR and HVEM was not significantly different expressed on CD8 +T cells in SLE.

**Conclusions** The costimulatory maker PD-1 is upregulated on cytotoxic T-cells in SLE. Further investigations are needed to elucidate the functional role of this pattern.