Objectives: Our objective here was to analyse a clinically well-phenotyped patients using a suite of immune assessments and identify inter-relationships between these features as well as subgroups of patients who may differ in response to therapy.

Methods: 143 SLE patients were evaluated for clinical phenotype using BILAG-2004, autoantibodies using radioimmunoprecipitation [IP, University of Bath], two intereferon scores (IFN-Score-A and IFN-Score-B), flow cytometry for major circulating immune cell subsets, as well as the surface protein expression of tethelin on each subset, a cell-specific assay for IFN response. Unsupervised hierarchical clustering was used to define autoantibody subgroups. IFN scores (reflected dCT) were compared between the groups using multivariate models. Other variables were compared using Kruskal-Wallis test with pairwise comparisons.

Results: Using IP, 141 patients could be divided into five subgroups: U1RNP/Sm+ only (n=23), Ro60+ only (n=8), U1RNP/Sm+Ro60+ (n=6), Ro60+Ro52+La+ (n=11), Ro52+ (n=16) and other ANA (n=77). Antibody subgroups was strongly associated with IFN-Score-A (F=4.49, p<0.001). Expression was lowest for “other ANA”, intermediate for single antibody groups, and highest with multiple positive antibodies. Multivariate linear regression, including interaction terms among antibody types, revealed that Ro60 and U1RNP/Sm were the independent predictors of IFN-Score-A level (p=0.051 and 0.009 respectively). There was no association between autoantibody status and IFN-Score-B (F=0.973, p=0.438).

In flow cytometry, the U1RNP/Sm group was notable for significantly lower numbers of CD4-T-cells and memory-B-cells. Memory -B-cells were also lower in antibody-positive groups compared to “other ANA”. Tethelin expression was increased in antibody-positive groups, but to a similar extent on most cell subsets. Memory B cell tethelin was significantly higher in the groups with multiple positive antibodies.

U1RNP/Sm+ was associated with renal involvement (p=0.004). Mucocutaneous involvement was greater in the Ro60+Ro52+La+ group (p=0.037).

Conclusion: This cohort revealed relationships between immune features. U1RNP/Sm antibody was notable for defining a group of patients with a cluster of immune abnormalities, including the greatest elevation of IFN activity, greater abnormalities on flow cytometry and clinical renal involvement. This was independent to the IFN-Score-B high status that predicts better clinical response to rituximab (presented elsewhere at this conference). Future work in MASTERPLANS will investigate the significance of these subgroups for response to therapy.

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Objectives: The main goal of the study was to determine the relationship of CD4+CD25+FoxP3+Treg cells with clinical and immunological manifestations in SLE patients (pts).

Methods: Frequencies and absolute numbers of peripheral blood CD4+CD25+FoxP3+Treg cells were assessed in 21 healthy donors and 20 SLE pts (2012 SLICC classification criteria); (1M/19F); age 32±13 years; disease duration median (25–75 percentile) 5(1-10) years; SLEDAI2K<10 - 15(10-22) (14 pts), <10 – 7(6-8) (6 pts). All pts were treated with prednisone, hydroxychloroquine, azathioprine, mycophenolate mofetil, cyclophosphamide. CD4+CD25+FoxP3+ Treg cells and B-cell subsets were analyzed using multicolor flow cytometry.

Results: Compared with healthy donors, SLE pts demonstrated significant lower the absolute number of Tregs (0.05; 0.04-0.06 vs 0.03;0.02-0.05x10^9/L, p<0.036), with a high percentage of Treg (8.7,5.1-10.5 vs 12.0,8.6-17.0, p<0.02). The median percentage of Treg was lower in pts with acute SLE compared to chronic SLE pts (9.0,3.9-9.9 vs 13.5,12.7-18.7%, p<0.02). SLE pts with high activity had a lower frequencies of Tregs (10.2,8.5-15.0 vs 15.8,12.7-20.4%, r=0.51, p<0.05). Low count of Tregs correlated with elevated level of IgG (r=-0.52, p<0.05). Absolute number of Tregscorrelated negatively with percentage and absolute count of transitional (CD19+IgD+CD10+CD27+) B cells (r=-0.66 and r=-0.63, p<0.05).

Conclusion: Decreased amount of T regs in SLE is associated with high disease activity, acute course and expansion of autoreactive B cells.

REFERENCES:


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