33 ASSOCIATION OF THE LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) WITH HEALTH RELATED QUALITY OF LIFE

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10.1136/lupus-2017-000215.33

Background and Aims Systemic lupus erythematosus (SLE) is associated with significant impairment of health-related quality of life (HR-QoL). The Lupus Low Disease Activity State (LLDAS) definition has not been previously evaluated for association with patient reported outcomes. The objective of this study was to determine whether LLDAS was associated with better HR-QoL, and examine predictors of HR-QoL, in a large multiethnic, multinational cohort of SLE patients.

Methods HR-QoL was measured using the Medical Outcomes Study 36-item Short Form Health Survey (SF-36v2) in a prospective study of 1422 patients. Disease status was measured using SLE disease activity index (SLEDAI-2K), physician global assessment (PGA) and LLDAS.

Results Significant differences in SF-36 domain scores were found between patients stratified by ethnic group, education level, damage score, and with the presence of active musculoskeletal or cutaneous manifestations. In multiple linear regression analysis, Asian ethnicity ($p<0.001$), a higher level of education ($p<0.001$), younger age ($p<0.001$) and shorter disease duration ($p<0.01$) remained significantly associated with better physical component scores (PCS). Musculoskeletal disease activity ($p<0.001$) was negatively associated with PCS, and cutaneous activity ($p=0.04$) was negatively associated with mental component scores (MCS). Patients in LLDAS had better PCS ($p<0.001$) and MCS ($p<0.001$) scores and significantly better scores in multiple individual SF-36 domain scores. Disease damage was associated with worse PCS ($p<0.001$), but not MCS scores.

Conclusions Ethnicity, education, disease damage, and specific organ involvement impacts on HR-QoL in SLE. Attainment of LLDAS is associated with better HR-QoL.

34 COMPARISON OF REMISSION AND LUPUS LOW ACTIVITY STATE AS PREDICTORS OF ORGAN DAMAGE

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10.1136/lupus-2017-000215.34

Background and Aims Outcome measures that combine control of SLE activity and prednisone reduction are clinically relevant. A clinical goal in SLE is to reduce risk of long-term organ damage. We assessed whether two recently proposed disease activity outcomes were predictive of future damage.

Methods For each month of follow-up, we determined whether the patient was in Clinical Remission (as defined by the DORIS work group) or low lupus disease activity state (LLDAS) (as defined by Franklyn *et al.*). Clinical Remission was defined as a PGA <0.5, clinical SLEDAI=0 and no prednisone or immunosuppressants. Clinical Remission on Treatment allowed for prednisone<=5 mg/day and immunosuppressant use. LLDAS was defined as a SLEDAI<=4, PGA<=1.0, no major organ activity, and no new activity. LLDAS on treatment allowed for prednisone use<=7.5 mg/d and immunosuppressants. Damage was defined using the SLICC/ACR index.

Results There were 81 118 person-months observed among 2026 patients (92% female, 53% Caucasian, 39% African-American). Table 1 shows the rates of damage, per person month, in subgroups defined by Remission or LLDAS.

Damage rates were relatively low when LLDA was achieved at least 50% of the time. These rates were similar to those experienced by patients who met a more stringent treatment restriction with Remission on Treatment at least 50% of the time.

Conclusions The equivalence of LLDAS and DORIS remission on treatment is welcome news, as LLDAS on treatment >50% of the time is an easier goal to achieve (3 times more person-months observed in our cohort) and more realistic as a clinical trial outcome.

Abstract 34 Table 1

Percentage of Prior Months in:	Number of person-months observed	Number of months with an increase in SLICC/ACR damage	Rate of damage per 100 person months	Rate Ratios	P-values
Clinical Remission					
None	35,772	406	1.13	1.0 (Ref)	
Not none, but < 25%	14,358	102	0.71	0.60 (0.48, 0.75)	<0.0001
25% to 50%	6573	50	0.76	0.66 (0.46, 0.94)	0.023
50% to 75%	3845	27	0.70	0.63 (0.42, 0.97)	0.035
75%+	1,641	10	0.61	0.58 (0.30, 1.15)	0.12
Clinical Remission on Treatment					
None	16,491	250	1.52	1.0 (Ref)	
Not none, but < 25%	20,169	170	0.84	0.54 (0.44, 0.67)	<0.0001
25% to 50%	14,344	103	0.72	0.46 (0.36, 0.60)	<0.0001
50% to 75%	8396	54	0.64	0.43 (0.30, 0.60)	<0.0001
75%+	2,789	18	0.65	0.45 (0.27, 0.75)	0.0019
LLDAS					
None	30,366	343	1.13	1.0 (Ref)	
Not none, but < 25%	10,880	106	0.97	0.86 (0.69, 1.07)	0.18
25% to 50%	5012	40	0.80	0.70 (0.51, 0.98)	0.037
50% to 75%	8494	60	0.71	0.63 (0.48, 0.83)	
75%+	7,527	46	0.61	0.54 (0.40, 0.73)	<0.0001
LLDAS on Treatment					
None	7,656	117	1.53	1.0 (Ref)	
Not none, but < 25%	10,555	134	1.27	0.83 (0.65, 1.06)	0.14
25% to 50%	12,686	129	1.02	0.66 (0.51, 0.85)	0.0013
50% to 75%	18,151	133	0.73	0.48 (0.37, 0.61)	0.0010
75%+	13,141	82	0.62	0.40 (0.30, 0.54)	<0.0001

Parallel Session 18: Autoimmunity and the environment

35 A DIET HIGH IN FIBRE DIET CAN MODERATE INFLAMMATION AND KIDNEY PATHOLOGY IN A MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2017-000215.35

Background and Aims Systemic Lupus Erythematosus (SLE) is a complex, multifactorial autoimmune disease mediated by the deposition of immune complexes in tissues such as the kidney, skin and brain, with the ensuing inflammatory cascade driving progressive tissue damage and dysfunction. Mice lacking Lyn tyrosine kinase ($Lyn^{-/-}$ mice) develop an autoimmune disease similar to SLE, driven by dysregulation of the immune system, immune complex deposition in tissue and systemic inflammation culminating in progressive glomerulonephritis. The gut microbiome has been shown to have an immunoregulatory effect on the development of autoimmune and inflammatory diseases, in large part due to the production of short chain fatty acids from the fermentation of dietary fibre.
Methods To determine whether dietary fibre could moderate systemic autoimmune and inflammatory pathology, $Lyn^{-/-}$ mice and control C57BL6/J mice were fed a high fibre diet (HFD) or a standard control diet from weaning until 42 weeks old.
Results On the control diet, $Lyn^{-/-}$ mice developed dysbiosis, lymphopenia, splenomegaly from enhanced splenic myelopoiesis, hyperactivation of immune cells, and pathogenic IgG anti-dsDNA autoantibodies that deposited in the kidney glomeruli leading to glomerulonephritis. These hallmarks of inflammation and autoimmune disease were significantly reduced in $Lyn^{-/-}$ mice fed a HFD, indicating that dietary intervention is effective at dampening chronic systemic inflammation and glomerular pathology.
Conclusions These findings highlights the contribution of diet and the gut microbiome in regulating systemic immune responses and controlling autoimmunity, inflammation, and preventing the progression of immunopathology and suggests that fibre supplementation may improve outcomes for those living with SLE or other chronic systemic inflammatory diseases.

36 IDENTIFICATION OF DISEASE-ASSOCIATED GUT MICROBIOTA IN LUPUS-PRONE BAFF-TG MICE

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10.1136/lupus-2017-000215.36

Background and Aims Systemic lupus erythematous (SLE) is a heterogeneous autoimmune disease with environmental and genetic contributing factors. The gut microbiota (GM) interacts with the immune system to maintain homeostasis. However, microbiome dysbiosis has been shown to lead to the development of autoimmune diseases. We aimed to investigate the role of GM in SLE-prone BAFF-Tg mice and study the possible benefit of GM-targeted treatments.
Methods We used 16S metagenomics to compare the GM composition, before or after disease onset, and before or after treatment of established disease with several different fibre-enriched diets or antibiotics. Gut bacteria composition was identified by sequencing V3-V4 regions on an Illumina MiSeq platform in a 96-plex library configuration, and bioinformatics analysis was performed using QIIME software. Matching data on mouse disease levels was obtained by flow cytometry, autoantibody ELISA, and kidney histology.
Results BAFF-Tg mice exhibited distinct GM compositions compared to WT, both before and after disease onset, with certain families of bacteria expanded or replaced prior to disease progression. GM-targeted therapy by high-fibre dietary modulation or antibiotics reduced anti-dsDNA autoantibodies to undetectable levels.
Conclusions GM dysbiosis, of some particular bacterial species we identified, can be linked to the level of disease development in this lupus-prone mouse model. Therapeutic strategies targeting GM, including easily implementable dietary modulations and antibiotics, could be investigated further as novel avenues for treating and managing SLE.

Free Communications 1 – Biomarker discovery

37 TOWARDS PATIENT STRATIFICATION IN SYSTEMIC LUPUS ERYTHEMATOSUS USING BASELINE AUTOANTIBODY SIGNATURES

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10.1136/lupus-2017-000215.37

Background and aims Patients with systemic lupus erythematosus (SLE) have a wide spectrum of clinical manifestations and disease activity. This has made it extremely difficult to demonstrate superiority of novel treatments in clinical trials. Our goal is to establish an autoantibody classification system of SLE subgroups of which one represents a more homogeneous SLE population with active disease.
Methods We first established the global SLE autoantibody reactivity profile by comparing SLE serum samples with healthy controls. High-content profiling revealed an extended autoantibody repertoire with reactivity to cytokines, interferon (IFN) and IFN pathway proteins. Based on screens with >700 SLE samples, we designed the multiplex NavigAID SLE array consisting of 86 diagnostic and novel antigens.
Results Starting with 86 NavigAID SLE antigens we stratified SLE into five subgroups with reactivity towards distinct subsets of antigens. For example, patients with nephritis could be subclassified into two subsets according to the presence of anti-dsDNA or anti-neutrophil cytoplasmic antibodies (ANCA) revealing the heterogeneity of SLE. Reactivity to anti-IFN pathway proteins was associated with high disease activity, whereas patients with low disease activity had only few autoantibodies. We also found SLE patients who were tested positive for anti-nuclear autoantibodies (ANA), but did not exhibit the typical SLE reactivity profile. These patients may have been misclassified based on their positive ANA test result and maybe considered as potential outliers in clinical trials.