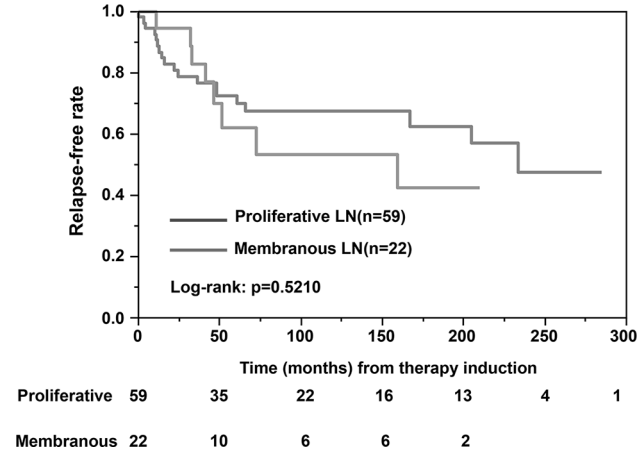

Abstract 36 Figure 1 Kaplan-Meier analysis cumulative for the renal relapse-free rate in proliferative and membranous LN

and 12 months after induction therapy, the relapse free period and life prognosis between proliferative and membranous LN.We need to closely follow up of therapeutic response and life prognosis of membrane LN as well as proliferative LN.

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37 ASSOCIATION OF SMOKING STATUS AND TOTAL AND INDIVIDUAL DAMAGE INDEX IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Smoking is a risk factor for systemic lupus erythematosus (SLE). It has been associated with increased disease activity and decreased effectiveness of hydroxychloroquine in cutaneous lupus. The objective of the study was to determine the association between smoking status and total and individual damage items in SLE.

Methods We analyzed data from the Hopkins Lupus Cohort. Damage was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index. Fishers exact test and Wilcoxon test were used in exploratory analysis. Logistic regression was used to estimate the association between damage and smoking status (ever/never). Odds ratios and 95% confidence intervals were reported. Stratification by ethnicity was done for individual damage items that were found to be significantly associated with smoking.

Results The prevalence of ever smokers in our cohort was 36%. SLE patients who ever smoked had higher odds of total damage with higher mean total damage index scores (p<0.0001). Data

Abstract 37 Table 1 Relationship between SLICC/ACR Damage Index Items and Smoking (ever/never)

	ALL		Caucasian		African American	
Damage Item	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Total damage	1.73 (1.44, 2.07)	< 0.0001	1.55 (1.22, 1.97)	0.0003	1.96 (1.44, 2.66)	<0.0001
Cataract	1.50 (1.17, 1.92)	0.00122	0.96 (0.68, 1.36)	0.8176	2.26 (1.56, 3.28)	<0.0001
Scarring alopecia	2.08 (1.42, 3.06)	0.00019	1.63 (0.60, 4.45)	0.3320	2.24 (1.46, 3.47)	0.0003
Extensive scarring or panniculum other than scalp	3.37 (1.95, 5.85)	0.0001	2.57 (1.01, 7.03)	0.0522	3.68 (1.90, 7.47)	0.00017
Skin ulceration	2.76 (1.37, 5.57)	0.00465	2.03 (0.8, 5.36)	0.1370	4.45 (1.48, 16.32)	0.0121
Pulmonary hypertension	1.53 (1.15, 2.03)	0.00367	1.11 (0.70, 1.75)	0.6430	1.79 (1.21, 2.63)	0.00334
Infarction or resection of bowels	1.42 (1.12, 1.79)	0.0032	1.37 (1.03, 1.84)	0.0338	1.36 (0.90, 2.04)	0.1461
Pancreatitis	3.57 (1.07, 11.88)	0.0382	2.44 (0.68, 8.67)	0.1694	N/C	N/C
Muscle atrophy	1.80 (1.11, 2.94)	0.0183	2.62 (1.26, 5.44)	0.0099	1.09 (0.54, 2.19)	0.8210
Coronary artery disease	2.26 (1.50, 3.41)	0.0001	2.33 (1.39, 3.91)	0.0013	2.35 (1.13, 4.89)	0.0226
Myocardial Infarction	2.30 (1.29, 3.32)	<0.0001	2.17 (1.30, 3.62)	0.0032	2.22 (1.27, 3.87)	0.0051
Cardiomyopathy	1.94 (1.29, 2.93)	0.0016	1.64 (0.81, 3.30)	0.1687	2.18 (1.27, 3.74)	0.0045
Claudication	4.53 (2.17, 9.48)	<0.0001	3.86 (1.47, 1.10)	0.0060	4.91 (1.55, 15.52)	0.0068
Cerebrovascular accident	1.41 (1.08, 1.84)	0.0127	1.16 (0.80, 1.69)	0.4279	1.69 (1.13, 2.54)	0.0115
Diabetes	1.72 (1.29, 2.28)	0.0002	1.33 (0.88, 2.03)	0.1764	2.08 (1.39, 3.12)	0.0004

N/C: data are not sufficient for calculating odds ratio

for individual damage items significantly associated with smoking are presented in table 1.

The association between cataract and smoking was still present after adjusting for ethnicity, diabetes, and prednisone use in a multivariate regression model (OR=1.4, p=0.0083).

Stratification by ethnicity showed that African- American SLE patients who ever smoked were more likely to have cataract, scarring chronic alopecia, extensive scarring, skin ulceration, pulmonary hypertension, cerebrovascular events, cardiomyopathy, and diabetes compared to non-smokers. Caucasian SLE patients who ever smoked were more likely to have extensive scarring, gastrointestinal infarction and resection, and muscle atrophy (table 1).

Conclusions Smoking is a modifiable factor for organ damage in SLE. It is already known that it interferes with the efficacy of hydroxychloroquine. Now we are able to prove that smokers have more cutaneous damage (scarring) even after stratification for ethnicity. As expected, smokers had more cardiovascular damage. New findings include associations with gastrointestinal damage, cataracts, pulmonary hypertension, pancreatitis and diabetes. In the general population, these associations have been confirmed in all except gastrointestinal infarction.

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38 REDOX-DRIVEN TYPE I INTERFERON IN SLE AND ITS TREATMENT WITH MITOQ

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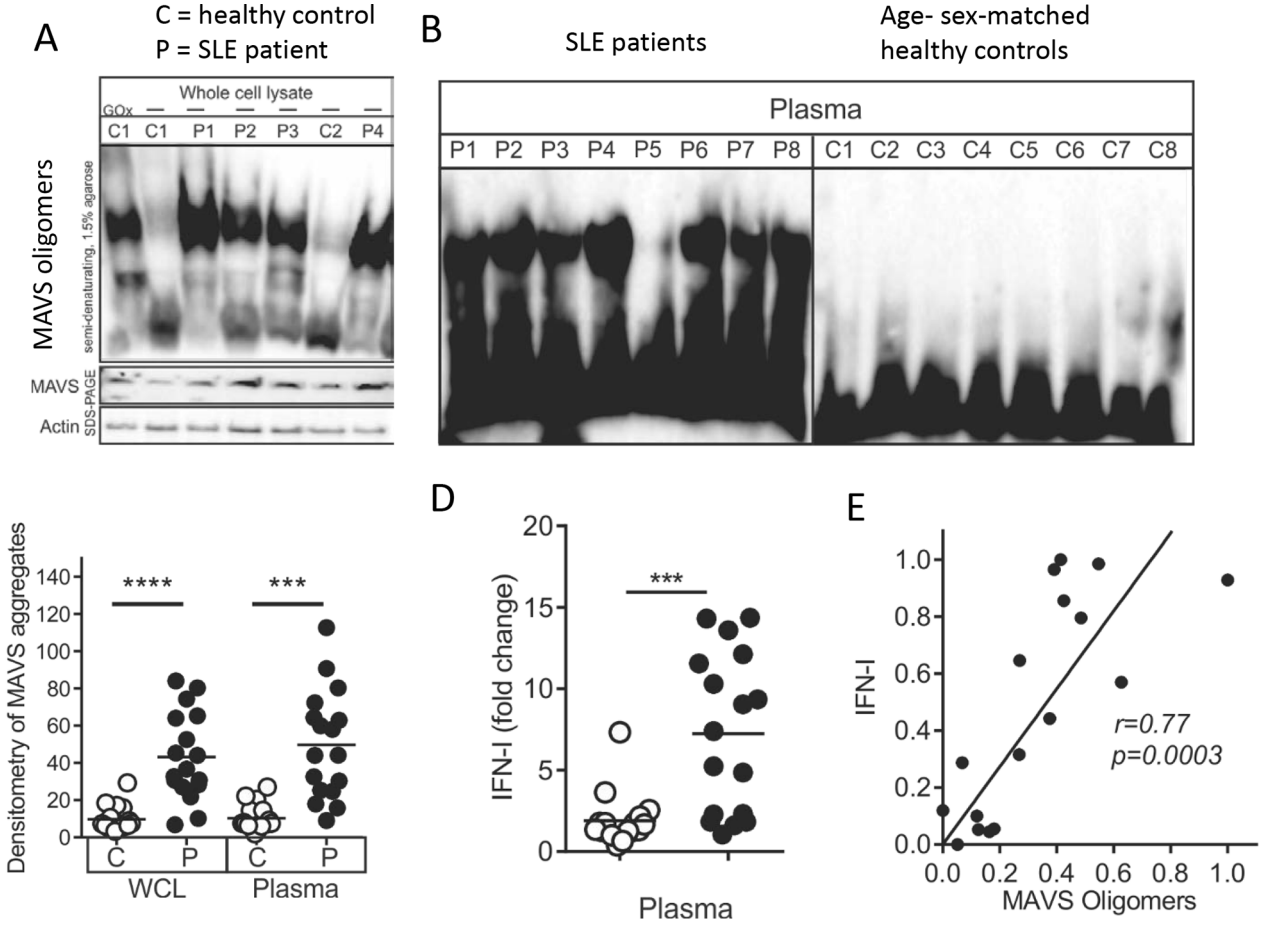
Background Systemic Lupus Erythematosus (SLE) is characterized by numerous seemingly unconnected abnormalities. These include: 1) a multisystem inflammatory syndrome, 2) a strong type I Interferon (IFN-I) gene signature in peripheral blood lymphocytes (PBL), 3) an unusual population of CD4-CD8- T-+cells, 4) SLE T cells containing enlarged mitochondria and reactive oxygen species (ROS), and 5) a polymorphism in Mitochondrial antiviral stimulator (MAVS C79F) associated with milder SLE. Our studies provide a unifying model for these abnormalities through augmented T cell homeostatic proliferation, which leads to two parallel cellular pathways: first, progressive upregulation of cytolytic inflammatory molecules, including high levels of Fas-Ligand (FasL), Granzyme B, and IFN-gamma, and second, generation of CD4-CD8- T cells from CD8 +precursors, which manifest disorganized enlarged mitochondria, elevated reactive oxygen species (ROS) that drives oligomerization of MAVS and IFN-I production.



Abstract 38 Figure 1 MAVS spontaneous oligomerization in SLE patients. (A and B) Whole-cell lysates (A) and plasma (B) of SLE patients (n=8 patients: P1 to P8) were analyzed by semi-denaturing agarose gel electrophoresis to detect MAVS oligomers. Healthy sex-, age-, and ethnicity-matched subjects served as controls (n=8 donors: C1 to C8). (C) MAVS oligomerization in whole-cell lysates (WCL) and plasma of SLE patients (black circles) and healthy control subjects (white circles) was quantified by densitometric measurement of Western blots. For WCLs, the ratio of MAVS monomer to oligomer was measured, whereas in plasma, MAVS oligomers were normalized to albumin abundance. (D) Type I IFN in plasma from control subjects and SLE patients were measured by ELISA. (E) The plasma concentrations of type I IFN and the degree of MAVS oligomerization in SLE patients were compared. The statistical analyses performed were independent t tests (for C and D). (***p<0.0005, ****p<0.00005)