

SUPPLEMENTARY MATERIALS

CELL-BOUND COMPLEMENT ACTIVATION PRODUCTS ASSOCIATE WITH LUPUS SEVERITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Calculation of the lupus severity index (LSI)

LSI was calculated using the following equation, as described (10).

$$\text{Lupus severity index} = \frac{k}{1 + \exp(-\sum j \hat{\beta}_j x_j)}$$

In the equation above, k is an arbitrary factor used to control the range of possible values of LSI. As this factor was set at 10 in this analysis, as described previously (10), LSI values can theoretically range from a minimum of 0 to a maximum of 10; x_j indicates a certain ACR criterion or sub-criterion and can be 0 (if a criterion is absent) or 1 (if a criterion is present); $\hat{\beta}_j$ is the coefficient used to weight each criterion or sub-criterion as described in Table S2 of Bello et al. (10).

For example, the LSI of a patient who fulfills the ACR criteria or subcriteria of malar rash ($\hat{\beta}_j = 0.020$), oral ulcers ($\hat{\beta}_j = 0.093$), arthritis ($\hat{\beta}_j = -0.289$), and immunologic ($\hat{\beta}_j = 0.447$), can be calculated as follows:

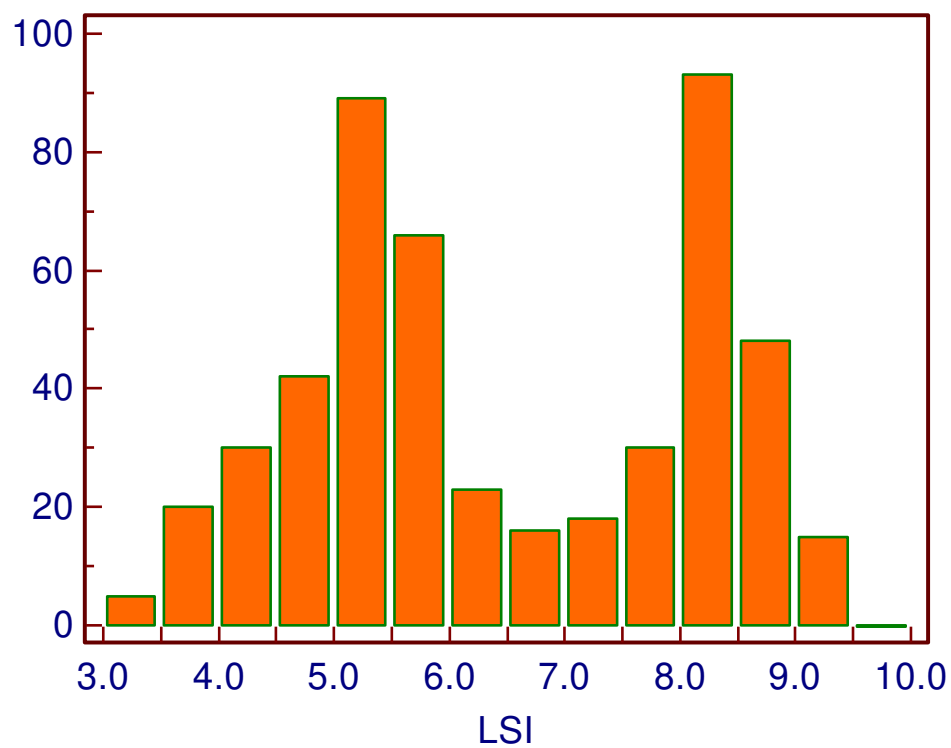
Multiply the criteria or subcriteria the patient presents with by their $\hat{\beta}_j$ and sum:
(1x0.020) + (1x0.093) + (1x(-0.289)) + (1x0.447) = 0.271; make the negative of

that value = -0.271; elevate e to the power of that value: $2.781^{(-0.271)} = 0.7626$;

add 1: $1 + 0.7626 = 1.7626$ and divide 10 by that number:

$$\text{LSI} = 10 / 1.7626 = \mathbf{5.67}$$

Supplementary Figure 1. Distribution of LSI within the patient population.



Supplementary Table 1: Association of LSI with elevated CB-CAPs, race, gender, complement, age, and disease duration (time since diagnosis), as determined by stepwise multivariable analysis. The model found that gender and low complement (low C3 and/or C4) were not significant when controlling for the other variables ($p=0.068$ and $p=0.067$, respectively); however, they are included in the final model ($R^2 = 0.156$) to determine their effect on CB-CAPs. Inclusion of these parameters in the model led to a minimal parameter estimate reduction for CB-CAPs, which remained strongly significant ($p<0.0001$).

Supplementary Table 1
Multivariable Model

Factor	Parameter Estimate	Standard Error	95% CI	p-value
Gender				
Male	0.438	0.240	-0.033 to 0.909	0.0684
Female	ref			
Race/Ethnicity				
Asian	0.592	0.172	0.059 to 1.126	0.0295
Black/African American	0.465	0.172	0.127 to 0.803	0.0071
Hispanic/Latino	0.390	0.196	0.005 to 0.776	0.0471
Other	0.457	0.439	-0.405 to 1.320	0.298
White/Caucasian	ref			
Low C3 and/or C4	0.279	0.152	-0.020 to 0.577	0.0671
Age at Visit	-0.022	0.006	-0.033 to -0.010	0.0002
Time Since Diagnosis	0.032	0.008	0.016 to 0.049	0.0001
Elevated CB-CAPs	0.636	0.152	0.337 to 0.935	<0.0001

Supplementary Table 2: Association of LSI with elevated CB-CAPs, race, gender, age, disease duration (time since diagnosis), and use of immunosuppressant medications in the subset of patients for whom medication information was available (n=438). Complement, anti-dsDNA, use of corticosteroids, and use of hydroxychloroquine were not significant when controlling for other covariates and are therefore not in the final model ($R^2 = 0.208$).

Supplementary Table 2
Multivariable Model

Factor	Parameter Estimate	Standard Error	95% CI	p-value
Gender				
Male	0.555	0.246	0.071 to 1.039	0.0246
Female	ref			
Race/Ethnicity				
Asian	0.515	0.286	-0.047 to 1.077	0.0724
Black/African American	0.533	0.175	0.189 to 0.877	0.0024
Hispanic/Latino	0.503	0.208	0.095 to 0.911	0.0157
Other	0.454	0.462	-0.455 to 1.363	0.3267
White/Caucasian	ref			
Age at Visit	-0.019	0.006	-0.031 to -0.008	0.0012
Time Since Diagnosis	0.025	0.009	0.007 to 0.042	0.0051
Elevated CB-CAPs	0.709	0.152	0.409 to 1.008	<0.0001
Use of Immunosuppressants	0.727	0.143	0.445 to 1.009	<0.0001

Supplementary Table 3: Subset analysis of patients for whom SELENA-SLEDAI renal activity parameter information was available (n=446). The data set did not include laboratory data. Association of LSI with elevated CB-CAPs, age, disease duration (time since diagnosis), and SELENA-SLEDAI renal activity. Race, gender, complement, and anti-dsDNA were not significant when controlling for other covariates and are therefore not included in the final model ($R^2 = 0.296$).

Supplementary Table 3
Multivariable Model

Factor	Parameter Estimate	Standard Error	95% CI	p-value
Age at Visit	-0.016	0.005	-0.027 to -0.006	0.0014
Time Since Diagnosis	0.024	0.008	0.008 to 0.040	0.0028
Elevated CB-CAPs	0.702	0.142	0.423 to 0.980	<0.0001
SLEDAI Renal Activity	1.937	0.198	1.549 to 2.326	<0.0001

Supplementary Table 4: Subset analysis of patients for whom medication and SELENA-SLEDAI renal activity parameter information was available (n=402). Association of LSI with elevated CB-CAPs, age, SELENA-SLEDAI renal activity, and use of immunosuppressants showed that race, gender, complement, anti-dsDNA, use of corticosteroids, and use of hydroxychloroquine were not significant when controlling for other covariates and are therefore not included in the final model ($R^2 = 0.319$).

Supplementary Table 4
Multivariable Model

Factor	Parameter Estimate	Standard Error	95% CI	p-value
Age at Visit	-0.007	0.005	-0.017 to 0.002	0.1401
Elevated CB-CAPs	0.760	0.145	0.474 to 1.045	<0.0001
SLEDAI Renal Activity	1.847	0.208	1.439 to 2.256	<0.0001
Use of Immunosuppressants	0.510	0.139	0.236 to 0.783	0.0003

Supplementary Table 5: Association of LSI with elevated CB-CAPs, race, gender, complement, age, and disease duration (time since diagnosis), as determined by stepwise multivariable analysis. The model found that gender, low complement (low C3 and/or C4), and dsDNA were not significant when controlling for the other variables ($p=0.0673$, $p=0.0964$, and $p=0.6160$, respectively); however, they are included in the final model ($R^2 = 0.157$) to determine their effect on CB-CAPs. Inclusion of these parameters in the model led to a minimal parameter estimate reduction for CB-CAPs, which remained strongly significant ($p<0.0001$).

Supplementary Table 5
Multivariable Model

Factor	Parameter Estimate	Standard Error	95% CI	p-value
Gender				
Male	0.440	0.240	-0.031 to 0.912	0.0673
Female	ref			
Race/Ethnicity				
Asian	0.595	0.272	0.061 to 1.128	0.0291
Black/African American	0.452	0.174	0.110 to 0.794	0.0097
Hispanic/Latino	0.386	0.196	0.000 to 0.772	0.0500
Other	0.437	0.442	-0.431 to 1.304	0.3231
White/Caucasian	ref			
Low C3 and/or C4	0.260	0.156	-0.047 to 0.567	0.0964
Anti-dsDNA positivity	0.082	0.162	-0.238 to 0.401	0.6160
Age at Visit	-0.021	0.006	-0.033 to -0.010	0.0002
Time Since Diagnosis	0.032	0.008	0.016 to 0.049	0.0002
Elevated CB-CAPs	0.620	0.155	0.315 to 0.926	<0.0001

Supplementary Table 6: The association of LSI with CB-CAPs is detailed with the parameter estimate, 95% Confidence Interval, and *p*-value, first noting the unadjusted univariate result. The next column details the CB-CAPs estimate as part of the final multivariable model that includes only significant predictors (Model 1 = CB-CAPs, Race, Age, and Disease Duration). Additional predictor variables are added to Model 1 to demonstrate the effect they have on the relationship between CB-CAPs and LSI. Please note that these variables are not available for all included patients, therefore Model 3, 4, and 5 are all analyses on a subset of the original patients (total for each model is indicated). Model 2 = Model 1+ Gender, Low Complement, anti-dsDNA, Model 3 = Model 2 + renal SLEDAI, Model 4 = Model 3 + Use of Immunosuppressants, and Model 5 = Model 4 + Use of Hydroxychloroquine and Use of Glucocorticoids (overall, Model 5 = CB-CAPs, Race, Age, Disease duration, Gender, Low Complement, Anti-dsDNA, renal SLEDAI, Use of Immunosuppressants, Use of Hydroxychloroquine, and Use of Glucocorticoids).

Supplementary Table 6
Multivariable Model
Elevated CB-CAPs and LSI

	Unadjusted (n=495)	Model 1 (n=495)	Model 2 (n=495)	Model 3 (n=446)	Model 4 (n=402)	Model 5 (n=402)
CB-CAPs						
Estimate	0.958	0.697	0.620	0.618	0.635	0.630
95% CI	0.672 to 1.244	0.406 to 0.987	0.315 to 0.926	0.324 to 0.911	0.330 to 0.939	0.320 to 0.940
<i>p</i>-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Model R²	0.081	0.145	0.157	0.310	0.343	0.346