

Supplemental Methods

Clustering Analysis

For flow-based clustering analysis, relevant populations were assessed as a percentage of total CD19+ cells across disease groups. Log-transformed population frequencies were assigned a z-score according to the mean and standard deviation of the subset as a whole. Patients were then clustered through Ward's method, as implemented by the R package, *pheatmap* (<https://cran.r-project.org/web/packages/pheatmap/>). Cluster grouping assignments were manually curated based on clear separation in the clustering analysis.

Luciferase Immunoprecipitation System (LIPS)

Protein luciferase fusion protein were produced by transfection of Cos1 cells with plasmids SmD3_LUC, RNPU1_70k_LUC, SSB/La_LUC, Ro60_LUC and Ro52_LUC. 1 µl of patient serum was mixed with 1.5×10^5 light units (LU) of fusion protein in buffer A (50 mM Tris, pH 7.5, 100 mM NaCl, 5 mM MgCl₂, 1% Triton X-100) and incubated for 1 hour with shaking. Subsequently, the mixture was transferred to MultiScreenHTS BV Filter Plates (Millipore Sigma), and incubated for 1 hour with shaking with Protein A/G UltraLink® Resin (Pierce™, ThermoFisher scientific). Precipitated auto-antigen luciferase fusion proteins were detected using the Renilla Luciferase Assay System (Promega). Known positive patient serum were used to establish a relative unit standard curve to normalize between assays.

9G4 IgG, 9G4 IgM and 9G4 IgA ELISA.

Polysorp 96-well plates (Nunc, Rochester, NY) were coated with 0.5 µg/ml rat anti-human 9G4 and then blocked with SuperBlock™ Blocking Buffer. Serum samples were added in serial two-fold dilutions starting 1:8000 (9G4 IgG), 1:1000 (9G4 IgM or 9G4 IgA). Bound serum antibody were detected by alkaline phosphatase-conjugated anti-human IgG (Sigma), IgM (Jackson ImmunoResearch Inc) or IgA (Sigma) antibody, in dilutions according to manufacturer's recommendations. 9G4+ positive serum IgG was quantified by monoclonal 9G4+ IgG standard curve, and 9G4+ IgM and IgA were quantified as arbitrary units based on a standard curve from SLE patients with known reactivity.

Apoptotic cells binding assay.

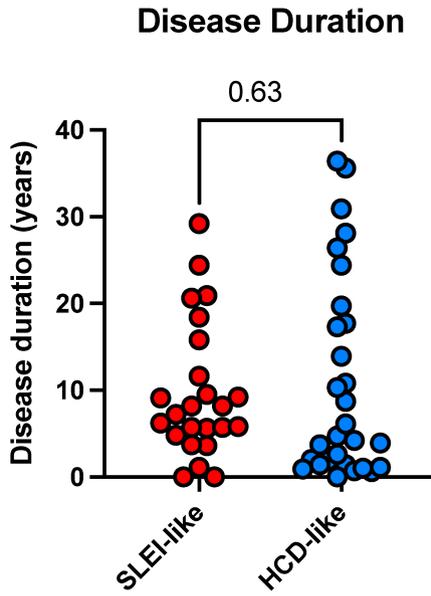
CD45-negative Jurkat cell line (J45.1; American Type Culture Collection) cells were incubated 18 h with camptothecin (20µg/ml) to induce apoptosis. Subsequently 3x10⁶ cells/50 µL were incubated with 25µl patient serum, followed by staining with 9G4 conjugated to Pacific Blue and 7-Aminoactinomycin D (7-AAD). Flow cytometric analysis was performed on a Cytoflex cytometer (BD Biosciences) late apoptotic cells were gated based on high 7-AAD expression and low forward scatter and 9G4+ antibody binding was quantified as mean fluorescence intensity (MFI). Known positive (SLE) and negative (HCD) serum samples were used in each experiment as controls.

Supplemental Table 1. Antibodies used for flow cytometry

Marker	Fluochrome	Clone	Source
CD19	APC-Cy7	SJ25C1	BD Biosciences
CD138	APC	44F9	Miltenyi
CD3	PerCP-Cy5.5	SP34-2	BD Biosciences
IgD	FITC	IA6-2	BD Biosciences
CD27	BV605	L128	BD Biosciences
L/D	eFluor506		eBioscience
9G4	PacBlue	9G4	F. Stevenson
CD38	PE-Cy7	HIT2	eBioscience
CD21	PE-Cy5	B-ly4	BD Biosciences
CD24	PE-A610	SN3	ThermoFisher
CD11c	PE	B-ly6	BD Biosciences

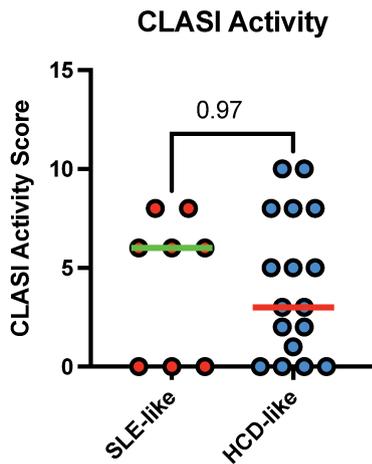
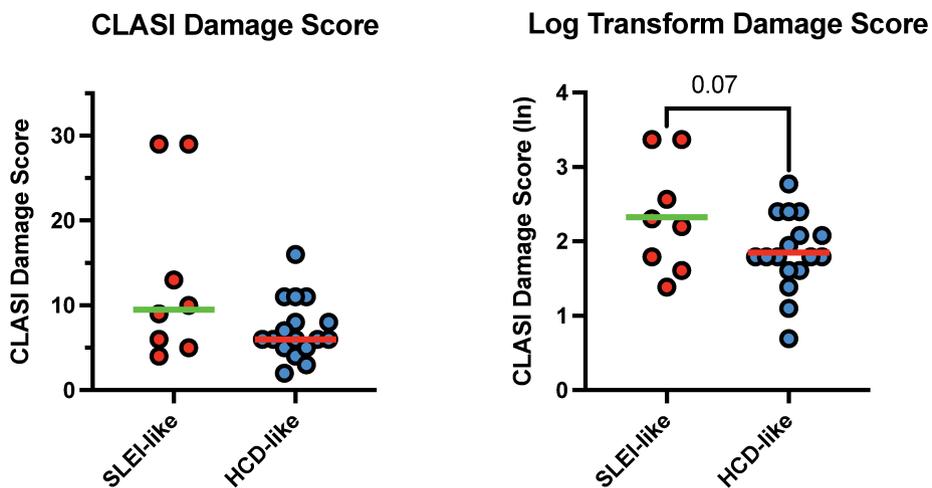
Supplemental Figure 1.

A.



Supplemental Figure 1. Disease duration does not differ between CCLE patients with SLE-like or HCD-like B cell phenotypes. The time between CCLE diagnosis and blood collection for flow cytometry is measured in years, $p=0.63$ Mann-Whitney test.

Supplemental Figure 2.

A.**B.**

Supplemental Figure 2. Skin activity and damage by B cell phenotype. A. The CLASI activity score ranged between mild to moderate activity in both groups, median score is indicated by the color lines (Mann-Whitney, $p=0.97$). B CLASI damage score is shown on the left with median indicated. The natural log transformed CLASI damage score is shown on the right; the mean damage score, indicated by color lines, was higher in the SLE-like group, although the difference was not statistically significant (t-test, $p=0.07$).