Abstract AI-19 Figure 1

helper function. The strong and specific positive correlation between Tph cell and CD21^{low} B cell frequencies suggests that these cells may act coordinately in the pathologic autoimmune response in SLE.

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Auto Antibodies

AA-01 PHENOME-WIDE ASSOCIATION STUDIES UNCOVER HIERARCHY OF AUTOANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Systemic lupus erythematosus (SLE) is a heterogeneous disease with diverse presentations. dsDNA antibodies associate with renal disease. Less is known about comorbidities in SLE patients without dsDNA antibodies. Using a large electronic health record (EHR) cohort, we sought to identify comorbidities that associate with dsDNA status. We used a technique that scans across EHR billing codes called phenome-wide association study (PheWAS) to compare SLE patients with and without dsDNA antibodies. We also evaluated the relative importance of SLE specific autoantibodies on SLE criteria.

Methods We used our validated SLE algorithm of ≥ 4 counts of the SLE ICD-9 code and ANA positive $\geq 1:160$ while excluding dermatomyositis and systemic sclerosis ICD-9 codes with a positive predictive value of 94% and a sensitivity of 86%. We identified SLE cases in a de-identified EHR that contains over 2.8 million subjects. Autoantibody status was defined as ever positive for dsDNA, RNP, Smith, SSA, and SSB. PheWAS was performed in dsDNA positive vs negative SLE patients using logistic regression adjusting for current age and race. For multiple testing, a false discovery rate (FDR) p of 0.05 was used. We also performed logistic regression to

assess the impact of autoantibodies, age, sex, and race on SLE criteria.

Results We identified 1097 SLE subjects. As expected, dsDNA positive subjects, compared to dsDNA negative, were more likely to have renal codes including nephritis (OR=4.60, FDR $p=2.33 \times 10^{-9}$), renal failure (OR=2.30, FDR $p=1.85 \times 10^{-5}$), and end stage renal disease (OR=2.63, FDR $p=0.01$). After adjusting for sex, race, age, and other autoantibodies, dsDNA was independently associated with nephritis ($p=1.98 \times 10^{-6}$) and chronic kidney disease ($p=0.001$) and also associated, along with SSB, with serositis ($p=0.01$) and hematologic criteria ($p=0.001$) (figure 1). dsDNA negative subjects were more likely to have codes for sleep, pain, and mood disorders.

Conclusion Using PheWAS, we uncovered a hierarchy within SLE specific autoantibodies where dsDNA, compared to other autoantibodies, was a powerful predictor of major organ involvement in SLE.

Abstract AA-01 Figure 1 Forest plots of logistic regression models for SLE criteria. Logistic regression models for nephritis (A) chronic kidney disease (B) serositis (C) and hematologic criteria (thrombocytopenia, pancytopenia) (D) were created with covariates shown on the left. Odds ratios are across the bottom with horizontal lines depicting 95% confidence intervals.