CD11C-HI T-BET+ B CELLS CONTRIBUTE TO THE PATHOGENESIS OF SLE THROUGH GENERATION OF AUTOREACTIVE PLASMA CELLS


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Background The etiology of systemic lupus erythematosus (SLE) is unclear, though dysregulated B cells play a key role. Several unconventional B cell subsets that associate with autoantibodies have been described in SLE. The aim of this study was to further evaluate B cell subsets in SLE and their connection to autoreactive specificities and disease manifestations.

Methods The frequency and phenotype of CD11c+Tbet+B cells were determined by flow cytometry. Autoantibodies were measured at the UT Southwestern core facility. The presence of CD11c+B cells in nephritic kidney was determined with IHC. IgH repertoires and mutational frequencies as well as transcriptome profile of CD11c+B cells were analyzed from RNA isolated from CD11c+B cells from SLE patients and compared to other B cell subsets from the same individual. Purified B cells from HD or SLE donors were cultured with either CD3-activated T cells or IL-21 co-stimulation and evaluated for B cell phenotype or production of auto-antibodies.

Results We found a CD11c hi T-bet +B cell subset highly expanded in SLE with a unique expression profile including chemokine receptors consistent with migration to target tissues. Notably, these cells were enriched for autoreactive specificities, present in nephrotic kidney and significantly correlated with specific clinical manifestations. IL-21 was a potent inducer of CD11c hi T-bet +B cells that further promoted the differentiation of these cells into Ig-secreting plasma cells. IgH repertoire analysis showed CD11c hi T-bet +B cells displayed a diverse repertoire with high levels of somatic hypermutation similar to memory B cells and plasma cells. This diverse repertoire suggests that CD11c hi T-bet +B cells accumulate in response to a plethora of antigens overtime, including self-antigens in SLE.

Conclusions These results show that CD11c hi T-bet +B cells are polyclonally expanded, and highly somatically hypermutated in SLE. Furthermore, IL-21 may be involved in their expansion and differentiation into autoreactive plasma cells, which in turn may contribute to autoimmune manifestations in SLE.

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SMOKING EXPOSURE IN PACK-YEARS PREDICTS CUTANEOUS MANIFESTATIONS OF LUPUS

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Background Patients of color are more likely to have systemic lupus erythematosus (SLE) and a smoking history. Prior literature notes that both smoking and race impact odds of cutaneous manifestations. Therefore, we sought to examine the impact of cumulative smoking and race on cutaneous manifestations of SLE.

Methods Our cohort study included 631 consecutive SLE patients at a single academic center. Adults with at least one ambulatory rheumatology encounter with an SLE ICD-9 or ICD-10 code from 2008–16 were identified. Electronic health records were manually abstracted to include patients meeting ACR 1997 or SLICC 2012 classification criteria. The primary outcomes were ACR or SLICC cutaneous criteria and SLICC Damage Index (DI) cutaneous criteria. The primary explanatory variable was smoking exposure defined as low (<5 pack-years), medium (5–10 pack-years), and high (>10 pack-years),...