expansions almost all B cells (80%) had a DN2 phenotype. DN2 cells predominate in African-American patients with active disease and nephritis, anti-Smith and anti-RNA autoantibodies. Among B cells, they express the highest levels of a T-bet/Zeb2 transcriptional network characteristic of effector T cells and lack the negative TLR regulator, TRAF5. Consistent with this transcriptional profile DN2 are hyper-responsive to TLR7. Moreover, DN2 cells share with activated naïve cells phenotypic, functional features, and a very similar transcriptome. When stimulated *in vitro* DN2 readily differentiated into plasma cells and produced autoantibodies.

Conclusions DN2 and activated naïve represent a separate B cell lineage with a distinct origin and function as they differed from other B cells subsets both in uniquely expressing several genes and a lack expression of other genes. This study defines a distinct differentiation fate of human autoreactive naïve B cells into effector plasma cell precursors with innate hyper-responsiveness to stimuli relevant to SLE, establishes the components and prominence of extrafollicular B cell activation in this disease, and identifies new therapeutic targets.

Abstract AI-07 Figure 1 A) representative flow profiles showing that IgD-/CD27-/CXCR5-/CD19++ DN2 B cells are rare in HCD but expanded in many SLE patients. B) the frequency of DN2 for HCD and 2 SLE patient cohorts as percentage of CD19+

AI-08 CHARACTERIZATION OF HUMAN AGE-ASSOCIATED B CELLS (ABCs) IN NORMAL AND LUPUS PERIPHERAL BLOOD

Jennifer L Barnas*, Jennifer Albrecht, Nida Meednu, Lin Gao, Mary O'Connell, R John Looney, Jennifer H Anolik. *University of Rochester, Rochester, NY, USA*

10.1136/lupus-2018-lsm.8

Background Age-associated B cells (ABCs) are associated with autoantibody production in lupus-like mice. This population is expanded upon exposure to self-antigen and interferon- γ . ABCs in mice are identified as CD11c+, CD21- and T-bet+. However, the characterization of these cells and factors promoting their generation in human SLE is unclear. The purpose of this study was to define ABCs in human SLE patients and their association with interferon (IFN) status.

Methods Peripheral blood leukocytes were purified by density gradient centrifugation from 26 lupus patients with a range of disease activity (n=10 with flaring disease, n=16 controlled disease) and 6 normal healthy donors. Surface and T-bet intracellular antibody staining was analyzed in a blinded fashion by flow cytometry. A putative population of ABCs was defined as CD3- CD19+ CD11c+ CD21- cells. Samples were divided into groups regardless of disease status based upon percentage of B cells with putative ABC phenotype. B cell subset analysis

was completed on the groups expressing minimal ($\leq 2\%$), intermediate ($2\% - 7\%$), or high ($\geq 8\%$) levels of ABCs. In addition, the B cell subset distribution (switched memory, unswitched memory, total naïve, and CD27- IgD- double negative) and phenotypic markers (CXCR3, T-bet, CD24, IgD, and CD27) of putative ABCs were assessed. IFN- α , IFN- β , and IFN- λ levels were quantitated by ELISA from sera drawn at the same time.

Results Five samples were identified as having high putative ABC levels (range 8.4%–20.5% of B cells, mean 14.9%). These CD11c+CD21- CD19+CD3- cells were predominantly CD24- CD27- IgD-. Across all 32 samples, the percentage of putative ABCs positively correlated with percentage of T-bet+ B cells ($r=0.819$, $p=5.4 \times 10^{-9}$), IgD- CD27- (double negative) B cells ($r=0.59$, $p=0.0003$), and CD24-double negative cells ($r=0.74$, $p=8.72 \times 10^{-7}$) with a high degree of statistical significance. Paired serum samples had a range of type I and type III interferon levels (mean +SEM for all samples): 6.2 ± 2.1 pg/ml (IFN- α), 4.0 ± 0.6 pg/ml (IFN- β), and 44.1 ± 9.6 pg/ml (IFN- $\lambda 1$). Analysis including correlation between B cell subsets, interferon status, clinical features and disease activity is in progress.

Conclusions An expanded putative ABC population (CD11c+ CD21- CD19+ CD3-) was identified in a subset of human peripheral blood samples. This subset is positively correlated with IgD-CD27-CD24- B cells (DN2 cells), whose expansion has been described previously in lupus patients.

AI-09 T FOLLICULAR HELPER (TFH) CELLS ARE INCREASED IN ASYMPTOMATIC ANTI-NUCLEAR ANTIBODY (ANA)⁺ INDIVIDUALS AND APPEAR TO PLAY A ROLE IN EPITOPE SPREADING

^{1,2,3,4}Joan Wither*, ¹Nan-Hua Chang, ^{3,4,5,6}Sindhu R Johnson, ³Waleed Hafiz, ^{1,2}Kieran Manion, ^{1,2}Dario Ferri, ¹Ariana Karanxha, ¹Babak Noamani, ¹Dennisse Bonilla, ¹Sina Rusta-Sellehy, ⁷Larissa Lisnevskaja, ^{3,4}Zahia Touma, ^{8,9}Earl Silverman, ^{3,4}Arthur Bookman, ¹Carolina Landolt-Marticorena, ^{1,2}Yuriy Baglaenko. ¹Krembil Research Institute, University Health Network, Toronto, Canada; ²Department of Immunology, University of Toronto, Toronto, Canada; ³Division of Rheumatology, University Health Network, Toronto, Canada; ⁴Department of Medicine, University of Toronto, Toronto, Canada; ⁵Division of Rheumatology, Mount Sinai Hospital, Toronto, Canada; ⁶Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada; ⁷Lakeridge Health Services, Oshawa, Canada; ⁸Division of Rheumatology, Sick Children's Hospital, Toronto, Canada; ⁹Department of Pediatrics, University of Toronto, Toronto, Canada

10.1136/lupus-2018-lsm.9

Background The diagnosis of Systemic Autoimmune Rheumatic Diseases (SARD), including Systemic Lupus Erythematosus (SLE), relies on the presence of ANAs, many of which can be detected years before clinical manifestations. However, ANAs are also seen in healthy individuals most of whom will not develop SARD. A number of cellular immune changes are seen in SARD, and thus could constitute potential biomarkers/treatment targets for SARD, however it is not known at what point in disease progression these develop.

Methods Healthy ANA⁻ controls (n=32) and ANA⁺ ($\geq 1:160$ by immunofluorescence) participants with no (asymptomatic ANA⁺, n=61), at least one (UCTD, n=35), or meeting SARD classification criteria (n=59) were recruited. Peripheral blood cellular immunological changes were assessed by flow cytometry.