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+ CD21+ CD11c+ 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 (≤2%), intermediate (2%–7%), or high (≥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=5.4×10−9), IgD− CD27− (double negative) B cells (r=0.59, p=0.0003), and CD24− double negative cells (r=0.74, p=8.72×10−7) 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-λ). 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.
**Results** Consistent with previous reports, SARD patients had increased proportions of activated B cells (CD86$^+$ or CD95$^+$) and in the SLE patient subset there were increased proportions of plasma cells/plasmablasts, as compared to ANA controls. SARD patients also had reduced proportions of iNKT and IFN-γ producing cells, as well as, increased proportions of memory Tfh (Cd4$^+$Ccr5$^+$PD1$^+$) and T regulatory (Treg, Cd4$^+$Foxp3$^+$Helios$^+$) cells, especially in the SLE and Sjogren’s Disease patient subsets. In asymptomatic ANA$^+$ individuals and UCTD patients, similar increases in the proportion of activated B cells, Tfh, and Treg cells, and decreases in the proportion of iNKT and IFN-γ producing cells were seen to those in SARD. In asymptomatic ANA$^+$ individuals and SARD patients, the extent of serologic changes (number of specific ANAs detected by Bioplex® 2200 ANA screening system) positively correlated with activation in the switched memory B cell compartment and the proportion of Tfh cells, with the later being an independent predictor of serologic status in a multivariate analysis. However, significantly elevated levels of Tfh cells could still be seen in asymptomatic ANA$^+$ individuals who lacked specific ANAs. Consistent with a role for Tfh cell in ANA production there was a strong correlation between the proportion of Tfh and plasma cells in asymptomatic ANA$^+$ individuals. In preliminary studies, the majority of Tfh cells in asymptomatic ANA$^+$ and UCTD patients were Tfh2 cells, with a trend to increased proportions of Tfh2 cells and decreased proportions Tfh17 cells as compared to active SLE patients.

**Conclusions** Tfh cells appear to play an important role in the development of a positive ANA and in the epitope spreading that may accompany disease progression, and therefore constitute a promising target for treatment of early disease.

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**AI-11  THE KINASE INHIBITORY REGION OF SUPPRESSOR OF CYTOKINE SIGNALING-1 MODULATES AUTOINFLAMMATORY SKIN PATHOLOGY**

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**Background** Although aberrant antibody production is a lupus disease hallmark, abundant evidence implicates a dysregulated peripheral T lymphocyte repertoire in the onset and progression of lupus. Notably, the intracellular protein suppressor of cytokine signaling-1 (SOCS1) has been shown to regulate T lymphocyte effector functions and modulate lupus-like pathologies in rodent models. Significantly, peritoneal injection of a peptide (SOCS1-KIR), capable of mimicking SOCS1, was effective in mitigating T lymphocyte effector functions associated with lupus disease progression. Moreover, topical application of SOCS1-KIR ‘eyedrops’ was effective in mitigating experimental autoimmune uveitis. The peptide has been shown to function through the inhibition of the janus kinases Jak2 and Tyk2. We have previously shown that peritoneal injection of SOCS1-KIR inhibited lymphadenopathy in MRL lpr/lpr mouse model of spontaneous lupus that was correlated to decreased frequencies of interferon gamma producing memory T cells (Collins et al, 2018 (under revision)). In addition, the peritoneal injection of SOCS1-KIR also inhibited spontaneous lesion formation=In this study we test the hypotheses that SOCS1 modulates skin pathology and that topical application of the SOCS1-KIR peptide will have efficacy in the imiquimod induced lesion model.

**Methods** SOCS1 heterozygous mating pairs, sufficient and deficient of interferon gamma, were obtained from St. Jude and used to generate mice used in the experiment. Spontaneous skin lesions were assessed by histology. In addition, cytokine-neutralizing antibodies were administered to evaluate mechanisms promoting lesion formation. Imiquimod was administered in the presence or absence of SOCS1-KIR to mice sufficient and deficient in SOCS1. Lesion formation was subsequently assessed.

**Results** SOCS1 ± IFN gamma +/- mice, but not SOCS ±, or IFN gamma +/- spontaneously developed epidermal hyperplasia. The SOCS1 ±, IFN gamma skin lesions were heavily infiltrated with macrophages and IL17 producing T lymphocytes. In addition, imiquimod induced skin lesions were exacerbated on SOCS1 ± mice compared to WT. Significantly, the topical administration of SOCS1-KIR to imiquimod treated murine skin reduced epidermal hyperplasia, erythema, and scaling.

**Conclusions** Together these results suggest that a peptide mimic of SOCS1 may have value as a therapeutic for lupus through topical and/or systemic administration.

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