responders but a low type I IFN signature and higher TNF- α expression in both HCQ/QC-nonresponders and HCQ/QC-responders.

Conclusions An increased number of mDCs may contribute to HCQ-refractoriness and predict a better response to treatment with both HCQ and QC but do not contribute to HCQ/QC-refractoriness. The significant correlation between macrophages and CLASI scores in the HCQ/QC-nonresponders, a finding not seen in either HCQ or HCQ/QC-responders, may also indicate that macrophages are more involved in antimalarial-refractory skin disease. The difference between the responders and nonresponders is further confirmed by the cytokine staining and mRNA expression. Our data is an initial step in determining the activation pathways that account for the lack of response to antimalarials.

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II-10 ROLE OF MACROPHAGE-DRIVEN AUTOINFLAMMATION IN SLE

¹Shuhong Han, ¹Haoyang Zhuang, ²Pui Lee, ¹Lijun Yang, ¹Westley H Reeves*. ¹University of Florida, Gainesville, FL, USA; ²Boston Children's Hospital, Boston MA, USA

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Background Although SLE is a prototype of autoimmune (T cell/B cell-mediated) disease, there is increasing evidence implicating myeloid cells in its pathogenesis. We examined the role of macrophages (M Φ) in human SLE and the pristane-induced lupus model.

Methods Tissues of SLE patients and mice with pristane-induced lupus were examined by double immunohistochemistry. M Φ were analyzed by flow cytometry, phagocytosis assay, real-time PCR, Seahorse assay, and RNA-Seq. Mice were injected daily with the liver X receptor (LXR) agonist T0901317.

Results SLE patients' bone marrow contained numerous activated caspase-3⁺ apoptotic cells located outside of M Φ . In contrast, in leukemia patients undergoing bone marrow ablation prior to transplantation, all caspase-3⁺ cells were inside of M Φ , suggesting that lupus is associated with impaired clearance of apoptotic cells. M Φ in pristane-lupus took up fluorescently-labeled apoptotic cells poorly compared with controls. Studies in pristane-treated knock-out mice indicated that the induction of diffuse alveolar hemorrhage (DAH), a serious pulmonary complication of lupus, required opsonization of dead cells in the lung by 'natural' IgM (DAH absent in μ MT mice, restored by infusion of IgM), C3, and C3b receptors (absent in C3-/- and CD18-/- mice, prevented by complement depletion with cobra venom factor). DAH also was prevented by M Φ depletion (clodronate liposomes) but not neutrophil depletion (anti-Ly6G). M Φ in pristane-induced lupus exhibited features of classical activation (impaired phagocytosis of apoptotic cells, high glycolysis, low oxidative phosphorylation, increased HIF1 α expression, M1 surface markers, and TNF α production), whereas control M Φ from mice treated with mineral oil (do not develop DAH) were M2-like, with high phagocytic activity, low glycolysis, high OxPhos, increased LXR α expression, M2 surface markers, and IL-10 production. In both pristane-induced lupus M Φ and SLE patients' monocytes, we found low levels of the LXR α -regulated reverse cholesterol transporter ABCA1. We hypothesized that it might be possible

to treat DAH by 're-polarizing' M Φ using a synthetic LXR agonist. Consistent with that idea, pristane-treated mice receiving T0901317 did not develop DAH and M Φ from mice receiving T0901317 exhibited an M2-like surface phenotype and decreased TNF α production compared with controls.

Conclusions Our data suggest that lupus-associated DAH is partly an autoinflammatory response caused by sluggish clearance of apoptotic cells by M1-like M Φ and that certain clinical manifestations (e.g. DAH) can be treated by repolarizing M Φ using an activator of the transcription factor LXR α . Low levels of LXR-driven ABCA1 expression also may have implications for the therapy of atherosclerosis in SLE.

II-11 SIGLEC-1 MACROPHAGES AND THE CONTRIBUTION OF IFN TO THE DEVELOPMENT OF AUTOIMMUNE CONGENITAL HEART BLOCK

Robert Clancy*. New York University Langone Medical Center, New York, New York

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Background Given that diseases associated with anti-Ro such as SLE and Sjögren's syndrome associate with an upregulation of type I interferons, recent attention has focused on a potential role for IFN in the pathogenesis of congenital heart block (CHB). Based on the consistent demonstration of macrophages and multinucleated giant cells in areas of injury, it is relevant that Sialic Acid Binding Ig Like Lectin 1 (SIGLEC1), a receptor on monocytes/macrophages is upregulated by IFN. Functionally, Siglec-1 expressing macrophages might play an important role as effector cells in fibrosis. Accordingly, this study leveraged both autopsy tissue and freshly isolated macrophages from a fetal heart dying with CHB to address whether IFN- α contributes to the pathogenesis of CHB by regulating activated macrophages in affected cardiac tissue.

Methods Three approaches were taken to evaluate Siglec-1 expression. Transcriptomic analysis was performed on macrophages freshly isolated from a fetal heart dying with CHB at 19 weeks and a heart from an otherwise healthy electively terminated fetus using (DAPI negative cells with isolation by flow using antibodies to CD45). Immunohistochemistry was performed on another fetal heart dying with CHB. *In vitro* experiments utilized cultured healthy human macrophages transfected with anti-SSA/Ro-associated ssRNA as a proxy for the *in vivo* conditions.

Results Transcriptomes of the two hearts for each isolated leukocyte fraction were compared. By following 213 IFN inducible genes, there was enrichment of targeted transcripts in CHB vs control ($p=0.0001$) and SIGLEC1, which was 200-fold more abundant in CHB vs control and ranked among the top three differentially expressed candidates. In another fetal heart dying with CHB, Siglec1 staining as detected by antibody HPA053457 was prominent in areas of injury. By morphology, the two cell types expressing Siglec 1 were macrophages and dendritic cells. *In vitro* experiments were performed in accordance with previous laboratory work, in which a model of anti-SSA/Ro-associated injury exploits macrophages stimulated with the ssRNA component (hY3) of the SSA/Ro immune complex. IFN inducible genes (15 transcripts) were among the 30 most highly upregulated genes in hY3 stimulated conditions and SIGLEC1 was two-fold more abundant in CHB vs control. Given the enrichment of type I IFN-responsive genes in the macrophage transcriptome, a WISH cell line was selected to evaluate supernatants from

macrophages transfected with hY3. IFIT1 MX1, and EIF2AK2 transcripts were significantly increased in the WISH cells treated with hY3 macrophage supernatants, but not macrophage supernatants alone ($n=7$, $p=0.02$).

Conclusion These data now provide a link between IFN and the inflammatory and possibly fibrosing component of CHB and position Siglec-1 positive macrophages as integral to the process.

Living with Lupus

LL-01 SOCIAL DETERMINANTS OF TREATMENT ADHERENCE AND DISEASE SEVERITY AMONG PEOPLE LIVING WITH LUPUS IN A SMALL ISLAND DEVELOPING STATE: A REPORT FROM ST. LUCIA

¹Amanda King*, ¹Cleopatra Altenor, ²Catherine Brown, ²Ian Hambleton. ¹Bay Medical Centre, St. Lucia, West Indies; ²The George Alleyne Chronic Disease Research Centre, Caribbean Institute for Health Research, The University of the West Indies, Barbados, West Indies

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Background The occurrence of systemic lupus erythematosus (SLE) varies considerably worldwide, with documented high incidence rates among women of African descent. The clinical course is likely influenced by social determinants, including

socioeconomic position (SEP), yet findings remain inconsistent, with little information from the Caribbean diaspora. This study presents the epidemiology of SLE in St. Lucia for the first time, exploring the association of SEP and SLE medication adherence and disease severity.

Methods Data have been collected from the only specialist lupus clinic in St Lucia between 1995 and 2017. We explored the effect of selected markers of SEP on disease severity (yes/no), and treatment adherence (yes/no) using logistic regression, adjusting for the effects of age, sex and years since diagnosis at all times. We used education level (primary or secondary education, tertiary education) or patients eligible for treatment cost discount or exemption (yes/no) as indicators of SEP. We also explored the effect of enrolment in a self-help programme on both regression outcomes, and the effect of treatment adherence on disease severity.

Results 143 people with SLE have been registered at the clinic between 1995 and 2017. The mean age at diagnosis was 32 years (standard deviation 12 years), and 132 (92%) were female, for a female to male ratio of 12 to 1. Since 2010 (a period of full clinic operation) 66 women have been diagnosed with SLE, for a crude incidence rate of 9.3 per 1 00 000 person years (95% CI 7.2 to 11.8). Half (49%) had a severe clinical course, defined as having cerebritis, nephritis, or being on dialysis, and half (50%) were medication adherent at their last follow-up visit. Higher SEP was consistently associated with increased treatment adherence and decreased disease severity (treatment adherence odds ratios ranged from 2.4 to 3.4; disease severity odds ratios ranged from 1.0 to 3.5) (figure 1).

Conclusion In St Lucia, among a population of predominantly African descent, and using selected markers of SEP, patients of lower socioeconomic position have more severe disease and lower medication adherence than those of higher socioeconomic position.

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LL-02 DEPRESSION IN PATIENTS WITH CHRONIC CUTANEOUS LUPUS ERYTHEMATOSUS: PREVALENCE AND ASSOCIATED FACTORS IN A PREDOMINANTLY AFRICAN AMERICAN COHORT FROM THE SOUTHEAST U.S

¹Jennifer Hong, ²Gaobin Bao, ³Tamara Haynes, ⁴Laura Aspey, ²S Sam Lim, ²Cristina Drenkard*. ¹Emory University School of Medicine, Atlanta, GA; ²Department of Medicine, Emory University School of Medicine, Division of Rheumatology, Atlanta, GA; ³Department of Medicine and Department of Psychiatry and the Behavioral Sciences, Emory University School of Medicine, Atlanta, GA; ⁴Department of Dermatology, Emory University School of Medicine, Atlanta, GA

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Background Chronic dermatologic diseases in general and cutaneous involvement in patients with systemic lupus erythematosus (SLE) in particular have been linked to increased depression. However, little is known about the burden of depression and its risk factors in patients with primary chronic cutaneous lupus erythematosus (CCLE), the most common type of cutaneous lupus. Additionally, previous studies examining CCLE have included predominantly white patients, despite recent findings indicating that black individuals have higher susceptibility for this condition and experience earlier damage in the disease course. We aimed to examine the prevalence of depression in patients with primary CCLE in the Southeast

Abstract LL-01 Figure 1 Odds ratios with 95% confidence intervals for potential predictors of disease severity and treatment adherence