Abstracts

Acknowledgements This work was supported by R01AI070304, K24AI078004, and the Lupus Research Institute.

II-09 IMMUNOLOGIC PROPERTIES OF CUTANEOUS LUPUS ERYTHEMATOSUS (CLE) PATIENTS REFRactory TO ANTimalarials COMPARED TO PATIENTS THAT RESPOND TO ANTimalarials

1,Krishna Desai, 1,Majid Zeidi, 1,2,3Hee Joo Kim, 1,2,3Victoria P Werth*. 1,2Corporal Michael J. Crescenz VAMC, Philadelphia, PA, USA; 3Department of Dermatology, Gachon University College of Medicine, Incheon, Korea

Background Two major therapies for cutaneous lupus erythematosus (CLE) are the antimalarials, hydroxychloroquine (HCQ) and quinacrine (QC). HCQ is often the first-line therapy for CLE, but only half of patients show a response to it. While some of the patients that do not initially respond to HCQ benefit from the addition of QC, there is a subset of patients that are refractory to both antimalarials. Refractoriness poses a huge challenge because these patients will often continue to have active disease when they are initially started on antimalarials. To better characterize these refractory patients, we investigated the immunologic characteristics of patients that respond to antimalarials versus those that do not.

Methods CLE patients were classified as HCQ-responders, HCQ/QC-responders, or HCQ/QC-nonresponders. Immunohistochemistry was used to characterize the inflammatory cell composition and cytokine expression in lesional skin biopsies from patients. Total RNA was extracted from these biopsies to analyze specific gene signatures. The patient’s CLASI score – a measure of disease activity – at the time of the biopsy was also determined.

Results Immunohistochemistry showed that myeloid dendritic cells (mDCs) were significantly higher in HCQ/QC-responders compared to HCQ-responders and HCQ/QC-nonresponders, while plasmacytoid dendritic cells, neutrophils, macrophages, and autoreactive T cells did not differ significantly among the three groups. The HCQ/QC-nonresponder group was distinct from the other groups in that their CLASI scores did correlate positively with the number of macrophages (p<0.05, figure 1). Staining also showed that IL-22 expression was significantly higher in HCQ/QC nonresponders versus the HCQ or HCQ/QC- responders while IL-17 expression was not significantly different between the responders and nonresponders. Analyzing the mRNA expression demonstrated a high type I IFN signature (LY6E, OAS1, ISG15, MX1) in HCQ-resistant patients.

Conclusions Both CR1 and CR2 levels are negatively associated with lupus disease activity in defined B cell subsets. Although this study does not prove causality, these data suggest that altered levels of these receptors on specific B cell subsets may predict disease flare or be associated with disease remission.
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.

Acknowledgements This work was supported by National Institutes of Health [K24 AR002207] and Veterans Affairs Merit Review [I01B × 000706] to Dr. Victoria Werth.

### Abstracts

**II-10  ROLE OF MACROPHAGE-DRIVEN AUTOINFLAMMATION IN SLE**

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

10.1136/lupus-2018-1sm.109

**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 (MΦ) 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. MΦ were analyzed by flow cytometry, phagocytosis assay, real-time PCR, Seahorse assay, and RNA-Seq. Mice were injected daily with the hydrogenated cholesterol (T0901317) agonist. Consistent with that idea, pristane-treated mice receiving T0901317 did not develop DAH and MΦ from mice receiving T0901317 exhibited an M2-like surface phenotype and decreased TNFα 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 MΦ and that certain clinical manifestations (e.g. DAH) can be treated by repolarizing MΦ using an activator of the transcription factor LXRα. Low levels of LXRα-driven ABCA1 expression may also 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

10.1136/lupus-2018-1sm.110

**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 anti-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...