responders but a low type I IFN signature and higher TNF-alpha 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 antimalarially 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.

---

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

1Shuhong Han, 1Haiyang 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-lsm.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 liver X receptor (LXR) agonist T0901317.

**Results** SLE patients’ bone marrow contained numerous activated caspase-3+ apoptotic cells located outside of MΦ. In contrast, in leukemia patients undergoing bone marrow ablation prior to transplantation, all caspase-3+ cells were inside of MΦ, suggesting that lupus is associated with impaired clearance of apoptotic cells. MΦ in pristane-lupus took up fluorescently-labeled apoptotic cells poorly compared with controls. Studies in pristane-treated knock-out mice indicated that 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.

---

**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-lsm.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...