Background: Cytoglobin (CYGB) is a non-erythroid globin that is found in medial smooth muscle cells (SMCs) of human vessels. Recent studies have postulated that CYGB act as a pro-survival factor during conditions associated with increased oxidative stress, by upregulating anti-apoptotic factors and antioxidant pathways. In this study, we hypothesized that CYGB regulates the inflammatory and antioxidant response associated with GCA pathogenesis.

Objectives: The purpose of this study is to evaluate giant cell arteritis (GCA) vascular lesions for the expression of CYGB and its association with specific molecular markers of cellular damage. We would also like to investigate the association of CYGB with GCA pathogenesis, symptomatic association of systemic inflammation, patient demographics, and response to treatment.

Methods: We obtained 29 temporal artery biopsy samples, 14-biopsy positive and 15-biopsy negative, from patients who underwent temporal artery biopsy for GCA diagnosis (Table 1). Inclusion criteria for the experimental group included patients over the age of 18 who had histologic evidence of GCA and met the ACR 1990 classification criteria. The control group included patients who were biopsy negative for GCA. Immunofluorescence staining for CYGB will be done on all samples to assess differential expression across the experimental and control groups. Proximity ligation assays (PLA) will be done to assess binding between cytoglobin and known pro-inflammatory markers to establish mechanistic insights for CYGB in the pathogenesis of GCA. We will also obtain clinical data including signs and symptoms at presentation, levels of serum inflammatory markers, treatment, clinical course, and outcomes.

Results: We are currently conducting validation studies of the immunofluorescence and PLA staining for specific molecular markers on temporal artery biopsy samples. Thus far, we were able to validate the immunofluorescence staining for CYGB (Figure 1) and the PLA for CYGB and HMGB2. Once we have established robust and reliable staining protocols for other markers, we will implement these protocols in our control and GCA groups and move forward with the analysis.

Conclusion: We previously demonstrated that overexpressing CYGB in human cardiac stem/progenitor cells (HCFPS) led to an increase in cell survival in response to oxidative stress. Whereas, silencing of CYGB in these cells increased the rate of cell death. Similarly in rat and mouse models, it was found that CYGB contributes to vascular remodeling following injury, and the absence of CYGB led to accelerated cell death and inhibition of neointima formation. Based on these studies, we hypothesized that CYGB may play a role in the pathogenesis of different vasculitises including GCA. Once we develop this correlation, we will use this data to identify cellular and serum markers for the diagnosis of GCA.[1, 2]

REFERENCES: