Role of COX-2 and 5-LO in mediating macrophage inflammatory response to *Borrelia burgdorferi* Ayan Farah, Christa D. Jackson, Charles R. Brown

Lyme disease, caused by an infection with the spirochete *Borrelia burgdorferi*, is the most prevalent vector- borne disease in the United States. During infection, arachidonic acid (AA) is metabolized by 5-lipoxygenase (5-LO) and cyclooxygenase-2 (COX-2) enzymes into immunoregulatory mediators known as eicosanoids. COX-2 creates one pathway by converting AA into prostaglandins, and the 5-LO pathway metabolizes AA to make leukotrienes. The goal of this project is to determine the effect of 5-LO and/or COX-2 inhibition on the macrophage response to *B. burgdorferi*. We expect to see that inhibition of 5-LO and COX-2 would lead to a decrease in pro-inflammatory cytokine production. To test this, RAW264.7 macrophages will be pre-treated with MK886 and/or CAY10404 to inhibit 5-LO and COX-2, respectively, followed by 24-hour co-culture with *B. burgdorferi*. After 24 hours, culture supernatants were assayed for TNF-α and IL-10 production by ELISA. We found that treatment with CAY10404 significantly decreased production of the pro-inflammatory cytokine TNF-α following *B. burgdorferi* co-culture. However, MK886 treatment had no effect on TNF-α production compared to the control. Further, dual treatment of macrophages with both inhibitors prior to co-culture yielded TNF-α production similar to CAY10404 alone. Neither treatment affected IL-10 production. Therefore, inhibition of COX-2 by CAY10404 significantly alters the macrophage cytokine response to *B. burgdorferi in vitro*. Future studies will focus on COX-2 response in RAW 264.7 macrophages, and this can set the stage for future experiments on the response of macrophages to this infectious agent.