Title: A study on three aspects of Inflammatory Bowel Disease's Triad of Susceptibility: Hormones, Helminths and T regulatory cells, in the Helicobacter hepaticus mouse model for IBD

Over 1.4 million American’s have been diagnosed with an Inflammatory Bowel Disease (IBD). The etiology of IBDs is unknown, however, it is believed that these diseases develop due to an inappropriate immune response to the microbiota driven by the complex interactions of an individual’s genetics, environment and immune system. The research presented here evaluates one aspect from each of the three susceptibility categories (genetics, environment and immune system) utilizing the H. hepaticus mouse model for IBD.

First, the effects of estrogen signaling on the development of IBD were evaluated in the A/J mouse; data from these experiments suggest when estrogen signaling is limited to ER-beta on a non-CD4+ cell population, disease severity is decreased. Next, the therapeutic potential of T. muris was evaluated in this microbiota driven IBD disease model. The data demonstrate that disease severity is acutely exacerbated and chronically unaltered by T. muris therapy in the A/J mouse. Lastly, the role T regulatory cells in the resistance to H. hepaticus-induced inflammation was examined through the use of neonatal thymectomies and diphtheria toxin treatments, which allowed for the depletion of natural T regulatory cells and Foxp3+ T regulatory cells in the C57BL/6 mouse. We demonstrate that neither the depletion of natural or inducible T regulatory cells at the time of H. hepaticus inoculation results in disease development.