

HORMONAL AND GENETIC REGULATION OF  
*HELICOBACTER HEPATICUS*-INDUCED  
INTESTINAL INFLAMMATION

Andrew Hillhouse

Dr. Craig Franklin, Dissertation Supervisor

ABSTRACT

Inflammatory Bowel Diseases (IBDs) affect millions of people worldwide and are characterized by a chronic intestinal inflammation resulting from a dysregulated immune response to environmental stimuli in genetically susceptible individuals. Utilizing a mouse model of IBD, the studies presented herein investigated 1) the role for estrogen and estrogen receptors in disease development 2) genetic factors contributing to differential disease susceptibility 3) differences in bacterial flora between susceptible and resistant mice. Infection of the A/J mouse strain with the bacterium *Helicobacter hepaticus* results in acute over-expression of proinflammatory cytokines followed 2-3 months later by chronic cecal inflammation that is more severe in females than in males. Studies in these mice investigating the role for estrogen and estrogen receptors have revealed that selective signaling through estrogen receptor  $\beta$  is immunomodulatory and decreases intestinal inflammation. *Helicobacter hepaticus* infected A/J mice develop intestinal inflammation, but infected C57BL/6 mice do not. Our investigations into the genetic factors responsible for *Helicobacter hepaticus*-induced intestinal inflammation have identified two major quantitative trait loci (QTL) on chromosome 3 and 17 associated with disease susceptibility. We also show that the microbial flora between these two mouse strains differs and can impact disease susceptibility. Together the work presented herein a further understanding into the role of hormones in controlling inflammation and insight into the genetic and bacterial factors associated with disease susceptibility.