POSTER 97

COORDINATE REGULATION OF *GATA3* AND CD4+ T-HELPER 2 (TH2) CYTOKINE GENE EXPRESSION BY THE RNA-BINDING PROTEIN HUR

Garrett M. Dahm (Doctoral Student)
Matthew M. Gubin (Doctoral Student)
Cristiana Stellato, MD, PhD (Professor, Johns Hopkins)
Joseph D. Magee, MD (Research Associate)
Xi Fang, PhD (Post Doc, Johns Hopkins)
Jinshui Fan, PhD (Post Doc, Johns Hopkins)
Vincenzo Casolaro, MD, PhD (Professor, Johns Hopkins)
Danielle M. Tarter, PhD
Jing Chen (Doctoral Student)
Glenn A. Jackson, DVM
Craig L. Franklin, DVM, PhD

(Ulus Atasoy, MD)
Departments of Surgery, Child Health, Molecular Microbiology and Immunology

Asthma and other allergic inflammation diseases are major contributors to hospitalizations and deaths worldwide. These diseases are the result of over reactive immune responses initiating pro inflammatory mediators. These CD4+ T helper type 2 (Th2) mediated diseases are driven by the transcription factor GATA3 as well as the cytokines IL-4 and IL-13. HuR, an RNA binding protein (RBP), has been shown to posttranscriptionally regulate many early response genes, including these critical allergy mediators. Specifically, GATA3 contains an AU-rich element in its 3' untranslated region (UTR), a putative binding site for HuR. When GATA3's 3' UTR is inserted into the highly stable β-globin mRNA, it significantly accelerates its decay in actinomycin D assays, suggesting it's role in GATA3's mRNA turnover. Furthermore, a knockdown of HuR in Jurkat T cells showed a significant decrease in GATA3 mRNA and protein levels as well as mRNA stability. To further understand HuR's role in GATA3 regulation and it's specific binding sites on its target mRNA, we designed probes for various sections of the GATA3 mRNA; GATA3 5' UTR, open reading frame (ORF) and 3 equal portions of the 3' UTR containing the putative binding domains of HuR. We will use these probes in immunoprecipitations to enrich for bound segments of GATA3 mRNA with HuR protein. We will then mutate the putative binding domains of HuR to analyze its effects on GATA3 regulation. Understanding HuR's regulation of GATA3 will be critical for fully understanding the development and progression of allergic inflammation and asthma in addition to its other important physiological roles.