UNC

SCHOOL OF MEDICINE

Microbiology and Immunology

DISSERTATION SEMINAR

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"The Role of Host Genetic Variation in Influenza A Virus Pathogenesis and Humoral Immunity."

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1131 Bioinformatics

Dissertation Advisor: Dr. Mark Heise

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ABSTRACT

Kelsey Noll: The Role of Host Genetic Variation in Influenza A Virus Pathogenesis and Humoral Immunity
(Under the direction of Mark Heise)

Influenza A virus (IAV) causes an acute respiratory disease, and is estimated to affect 50 million people annually in the United States alone. Among infected individuals, severity of disease varies greatly, from asymptomatic to severe and fatal cases. Likewise, efficacy of the IAV vaccine also varies across the population. Host genetic factors contribute to this variation, however they are challenging to study in humans due to the lack of experimental controls, biological replicates, and access to relevant tissues. We utilized the Collaborative Cross (CC), an experimentally tractable mouse genetic reference population, to study the role of host genetic variation in mediating disease and antibody response to IAV infection and vaccination. Through multiple experimental approaches, we demonstrated that heritable factors play an important role in driving host response to IAV, and genetically mapped quantitative trait loci (QTL) associated with variation in specific outcomes. We extended this analysis by considering relationships between QTL and other related phenotypes to gain further understanding of their breadth of effect and possible mechanisms. We also described a computational software tool to facilitate these types of analyses. Overall, this work provides valuable insights into the genetic regulation of host response to IAV, laying a framework of experimental design as well as a repository of QTL and data to benefit future studies in the CC and beyond. Ultimately, identifying specific genes that underlie variation in IAV infection and vaccine responses could drive optimized design of preventative and therapeutic care to improve global health.