“THE CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) CHANNEL AS A HOST DETERMINANT OF INFLUENZA SEVERITY”
VITA

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ABSTRACT

Influenza A virus is a readily transmissible respiratory pathogen that remains a significant threat to human health. Annual influenza epidemics are responsible for roughly 3 to 5 million cases of severe illness and more than 300,000 deaths/year worldwide. Additionally, the emergence of novel pandemic strains has the potential to cause devastating loss of life. Treatments for influenza infection, including vaccination and antiviral therapy, have limited utility. Vaccination plays a pivotal role in preventing influenza infection, but several issues arise related to vaccine uptake, distribution, and production. Moreover, a recent meta-analysis determined that antiviral drugs do very little to prevent influenza-related hospitalizations. Thus, there is a need for new therapeutics that can treat late-stage, severe influenza infection.

In severe cases, primary influenza infection can lead the development of pulmonary edema and hypoxemia: key features of acute lung injury (ALI). Influenza infection gives rise to ALI via two mechanisms: 1) The disruption of normal ion transport in the distal lung leading to pulmonary edema; and 2) The induction of an over-robust immune response leading to tissue damage. We have previously shown that influenza-induced ALI in C57BL/6 mice (WT mice) was associated with increased Cl- secretion via the cystic fibrosis transmembrane conductance regulator (CFTR) Cl- channel expressed on cells of the distal lung. Interestingly, C57BL/6-congenic mice that are heterozygous for the F508del mutation in CFTR (HET mice), which exhibit a 50% reduction CFTR expression and CFTR-mediated Cl- transport, experienced a significant attenuation in ALI. Thus, the aim of these studies was to identify various factors within the HET model that dictate the beneficial phenotype. Attenuated ALI was alveolar macrophage (AM) dependent and was not linked to alterations in viral replication between strains. Also, HET AMs displayed an anti-inflammatory phenotype compared to their WT counterparts. Elevated levels of the cytokines, TGF-β and IL-6, were observed in
the HET mice, and neutralization of these cytokines eliminated the beneficial phenotype. Lastly, using mice that were heterozygous for 2 additional CFTR mutations, we were able to determine that reduced CFTR expression, not CFTR-mediated Cl- secretion, may be most important in the attenuation of ALI. Taken together, these findings identify CFTR as a novel host determinant for influenza severity, and provide a rationale for modulating CFTR for therapeutic benefit.
RECENT ABSTRACTS AND PRESENTATION

College of Veterinary Medicine Graduate Student Seminar (2015)
Abstract: The Cystic Fibrosis Transmembrane Conductance Regulator is a Host Determinant of Influenza Severity.

Poster Presentation
Abstract Title: Alternatively Activated Macrophages Attenuate Influenza-induced Acute Lung Injury in Mice Heterozygous for the F508del mutation in CFTR.

Poster Presentation
Abstract Title: Alternatively Activated Macrophages Attenuate Influenza-induced Acute Lung Injury in Mice Heterozygous for the F508del mutation in CFTR.
RECENT PUBLICATIONS


*Co-first authorship
AWARDS AND HONORS

College of Veterinary Medicine Graduate Student Seminar- 1st Place Presentation (Fall 2015)

Award C. Glenn Barber Fund (2014-Present)

HHMI MED into GRAD Scholars Training Program (2013-2014)

OSUMC Trainee Research Day Travel Award (2014)

Biomedical Sciences Graduate Program Travel Award (2014)

FUTURE PLANS

I am currently finishing up the interview process for post doctoral fellowship positions. It looks like I will either be at the University of Chicago conducting research in pulmonary immunology or at Weill Cornell Medical College studying malarial pathogenesis.

My ultimate career goal is to obtain a position in which I can formulate and test my own hypotheses. An ideal environment for such an endeavor would be a position within the realm of academia. On the other hand, I am also open to careers in the private and government sector as long as the positions would grant me a certain level of intellectual freedom.