INTERDISCIPLINARY GRADUATE PROGRAM IN

IMMUNOLOGY

DISSERTATION SEMINAR

“NK cell responses control and define the sepsis-induced cytokine storm and immunoparalysis state”

Isaac Jensen
PhD Candidate

October 6th, 2020
2:00 p.m.
2117 MERF & via Zoom

NK cell responses control and define the sepsis-induced cytokine storm and immunoparalysis state

Sepsis is a dysregulated host response to systemic infection that leads to immunologic dysfunction and organ damage. This dysregulated host response, termed the cytokine storm, is composed of both pro- and anti-inflammatory cytokines that are detrimental or beneficial to host survival, respectively. While early intervention has improved survival of the acute cytokine storm, ~20% of people still succumb to the septic inflammation. Yet, even as survival of the cytokine storm has increased it has also become apparent that septic patients experience a prolonged state of immunologic dysfunction, termed immunoparalysis, that reduces host capacity to respond to secondary infections.

My thesis work focuses on NK cells to understand the interplay between cellular responses and the septic event, this is with respect to how NK cells both influence and are influenced by the cytokine storm. I demonstrate that, rather than being detrimental mediators of the cytokine storm, NK cells are critical regulators of the septic event and limit the cytokine storm through the production of the anti-inflammatory cytokine IL-10. This insight may promote the development of therapeutic intervention strategies to diminish the severity of the septic event by modulating NK cell activity.

Additionally, I characterized how sepsis leads to numerical and functional impairment of NK cells that defines the immunoparalysis state. Sepsis-induced functional impairment encompasses transcriptional changes that reduce NK cell capacity to respond to both cytokine and receptor stimulation. This culminates in a reduced host capacity to control infection. Promisingly, lymphoproliferative therapeutic intervention increased host capacity to control infection by increasing the number, but not intrinsic function of NK cells. This supports similar therapeutic strategies for alleviating the sepsis-induced immunoparalysis state.

Isaac Jensen
Biographical Sketch

Isaac was born in Bismarck, ND to William and Laura, and is the eldest of his 3 siblings Paul, Mark, and Ruth. Isaac has always had a passion for science.

With an interest in Microbiology and Immunology Isaac attended the University of North Dakota, where he majored in Biology with an emphasis in molecular and cellular biology. Through his faculty advisor Isaac was introduced to Dr. David Bradley and began working in Dr. Bradley's lab. While in Dr. Bradley's lab, Isaac's project interrogated a parasite-derived immunosuppressive agent in the suppression of a mouse model of arthritis. During the following 3-years in Dr. Bradley's lab Isaac developed several of the bench science skills that would later help him in graduate school. During his senior year of undergrad Isaac applied to and was accepted into the Immunology graduate program in 2015.

Isaac joined the lab of Dr. Vladimir Badovinac in May 2015, and has developed a keen interest in studying Natural Killer (NK) cell function in the context of both the sepsis-induced cytokine storm and immunoparalysis state. His work in the Badovinac lab also extends to several other cell types and disease states as they pertain to sepsis. Isaac values his time in lab and with his labmates, who are both great co-workers and friends. Beyond the bench, Isaac spends the majority of his time with his wife, Sam, while enjoying beer brewing and attending weekly trivia with his friends.

DISSERTATION COMMITTEE

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