THE OHIO STATE UNIVERSITY
INTEGRATED BIOMEDICAL
SCIENCE GRADUATE PROGRAM
SUMMER 2011

Dennis J. Horvath, Jr.
PhD Candidate

“The Impact of Phagocyte-UPEC Interactions Upon Pathogenesis of Urinary Tract Infections”

August, 22, 2011
Biomedical Research Tower Room 134
9:00 am
VITA

February 18, 1981 . . . . . . . . . . . . . . . . . . . . Born – Sylvania, OH

May, 2004 . . . . . . . . . . . . . . . . . . . . . . B.S., John Carroll University

COMMITTEE MEMBERS

Dr. Sheryl Justice

Dr. Santiago Partida-Sanchez

Dr. John Gunn

Dr. Stephanie Seveau

Dr. Larry Schlesinger

AWARDS AND HONORS

Travel Award Inaugural Imaging and Flow Cytometry Research Day For Outstanding Trainee Poster 2009

Finalist poster presentation at Research Institute at Nationwide Children’s Hospital Research Day 2010

FUTURE PLANS

Dennis is pursuing a postdoctoral research fellowship position in the laboratory of Dr. Holly Algood at the Department of Medicine at the Vanderbilt University Medical Center in Nashville, TN. Dennis will investigate the innate and adaptive immune response to Helicobacter pylori, a pathogenic Gram-negative bacteria. Specifically, Dennis will determine the role of T helper responses in control of infection and gastritis and investigate how T helper responses modulate ongoing innate immune responses to the bacterium.
RECENT PUBLICATIONS


ABSTRACT

Uropathogenic Escherichia coli (UPEC) is the principle causative agent of urinary tract infections (UTIs). UTIs are considered to be the most common bacterial infection and account for a large degree of medical expenditures in the United States. UPEC possess numerous strategies to evade the innate immune system including: suppression of pro-inflammatory cytokines, invasion into bladder epithelial cells, development of intracellular bacterial communities, and filamentation. Filamentation, growth in the absence of cell division, has been shown to be essential for UPEC pathogenesis in a murine cystitis model. Furthermore, filamentous Gram-negative uropathogens have been identified in the urines of women with cystitis. Filamentous UPEC promote bacterial persistence within the urinary tract by contributing to the development of additional rounds of intracellular infection and the formation of a quiescent intracellular reservoir. However, the mechanism(s) by which filamentous UPEC are elicited and evade phagocytic killing remain unknown. Here we determined that shape-based inhibition of phagocytosis is the mechanism whereby UPEC is able to evade phagocytic uptake.
and destruction. Furthermore, we demonstrated that co-culture of UPEC with murine phagocytes (bone-marrow derived macrophages, peritoneal neutrophils, peritoneal macrophages, and RAW 264.7 cells) and the human cathelicidin, LL-37, are sufficient to elicit UPEC filamentation in vitro. Also, we determined several two component systems (PhoPQ, PmrAB, SoxRS) mediate protection of UPEC from the induction of filamentation. Finally, we determined that CX3CR1^{low} macrophages and CX3CR1^{high} dendritic cells contribute to the clearance of UPEC from the kidneys. In conclusion, we have demonstrated that filamentous morphology provides UPEC with an additional mechanism to evade innate immunity and that macrophages and dendritic cells contribute to the antibacterial defense of the urinary tract.

RECENT ABSTRACTS AND PRESENTATION
Ohio University, Athens, Ohio, April 2011
Ohio Branch ASM Spring Meeting
Title: CX3CR1-hi macrophages are required for control of urinary tract infection in mice


Horvath, Jr., DJ, Li B, and Justice SS. (2010) Novel Mechanism of SulA induction during cystitis. The Ohio Branch Meeting of the American Society for Microbiology.