Personal Information

Last Name:Doore | Dept.:Biochemistry & Molecular Biology

First Name:Sarah | e-mail:sdoore@msu.edu

Supervisor: Kristin Parent | Supervisor e-mail:kparent@msu.edu

Conference Details

Communication Type: oral presentation (if selected) or poster | Date:8/5/2019

Total Expense (USD):$1,295 | Location:Madison, WI

Conference Title:Molecular Genetics of Bacteria and Phages

Communication Title: O-antigen modifications and herd immunity against phage attacks

ABSTRACT

For a virus to succeed at infection, it must first recognize a suitable host cell. Gram-negative bacteria have both outer and inner membranes, which contain a variety of membrane proteins. On the outermost surface of the outer membrane, there is an additional layer of lipopolysaccharide (LPS) that coats and protects the cell from harsh environments. Bacterial viruses, known as phages, typically go through at least two stages of host recognition. The first, reversible stage involves weak binding—commonly via lipopolysaccharide—to test whether a cell is the "correct" host. The virus then degrades LPS and enters the second, irreversible stage of attachment: binding to a secondary receptor, which is often a protein embedded in the outer membrane. This commits the phage to infection by triggering the movement of its genome out of the viral particle and into the host cell.

Podoviruses—phages with short tails—have tailspikes that bind to and degrades LPS, while another previously-unidentified protein interacts with the secondary protein receptor. Through a series of experimental evolution and targeted genetic studies, we determined that tailspikes are more complex than previously thought, and that LPS alone can inactivate phage particles prior to genome translocation. By evolving podovirus Sf6 to infect a new host, we found that the tailspike interacts with both LPS and the secondary protein receptor, making this the singular critical protein responsible for infection initiation. We also discovered that Sf6 specifically requires multiple components of LPS for infection, as disruption of genes in two independent LPS biosynthesis pathways completely block infection. Finally, we determined that LPS can be used as a passive weapon against phages. Even low levels of "incompatible" LPS will trigger viruses to prematurely lose their genomes, rendering them completely uninfectious. This may serve as community-level immunity for bacteria with significant ecological implications, as mixtures of susceptible and non-susceptible bacteria in an environment can reduce the overall presence of phages.

COMMUNICATION OUTCOMES

In the Parent lab, I have been investigating a number of aspects regarding phage biology. Phages—viruses that infect bacteria—have been critical model systems in a variety of scientific fields. In addition to their roles in basic biology, ecology, and genetics, these viruses are becoming medically relevant due to the current antibiotic resistance crisis. My research over the last couple of years has been focused on a subset of phages that infect Shigella flexneri, the causative agent of bacillary dysentery.

The work presented at this conference will have significant implications for phage biology and microbial ecology, as LPS has not been shown to serve as anti-phage defense, especially at a community-wide level. In addition, phage tailspikes were previously thought to only bind and degrade LPS, but my work indicates that it has multiple intertwined roles and participates in several types of interactions. The mutants isolated in this study also support a recently-developed model of the kinetics of phage-host interactions.

As a senior postdoc, attending this conference will help me network, find out about upcoming job openings, and establish new relationships within the microbial genetics community. Although I have attended phage/virus meetings in the past, I have not attended the Molecular Genetics of Bacteria and Phages conference. Being selected for an oral presentation at this meeting would be seen as quite prestigious, but even a poster presentation would give me additional exposure and be viewed favorably on my CV. I plan to apply for academic positions in the upcoming academic cycle, and this travel award will help me in two ways: 1) by giving me a chance to talk about my research to a broader audience; and 2) indicating that I take the responsibility of funding myself seriously.