Brian Pettygrove, PhD candidate in the Department of Microbiology & Cell Biology will present a dissertation defense titled "Characterization of Host-Pathogen Interactions During Early Staphylococcus aureus Biofilm Formation on Surfaces" on Thursday, March 31st from 1-2pm in Byker Auditorium.

ABSTRACT:

Implanted biomaterials such as orthopedic screws, prosthetic joints, pacemakers, and catheters are essential components of modern medicine. Unfortunately, implanted foreign bodies are susceptible to biofilm infection, leading to a persistent and difficult to treat disease state. Biofilm infections readily tolerate clearance from the immune system, however much of our understanding of the mechanisms governing persistence are formulated around the biofilm state during advanced infection. By comparison we have a poor understanding of the early stages of infection. Specifically, how contaminating organisms initially evade host immune defenses and establish a robust infection remains ill-defined. In this work, we interrogated interactions between Staphylococcus aureus (S. aureus), a frequent culprit in biomaterial infections, and early contributors to host immunity. Using in vitro time-lapse microscopy, we observed that human neutrophils readily phagocytose and kill single cells or small clusters of S. aureus cells that are attached to a surface. S. aureus cells that go undiscovered during the initial stages of neutrophil surveillance form biofilm aggregates that rapidly gain tolerance to neutrophil killing. In vivo models of implant infection demonstrated that surface adherent bacteria can evade discovery due to delayed or heterogeneous neutrophil recruitment to the surface. Biofilm aggregate formation was impaired in a strain deficient in the two-component gene regulatory system SaeR/S and the resulting cells were highly susceptible to neutrophil killing. Inhibition of aggregation was dependent on serum complement proteins C3 and factor B, suggesting that SaeR/S regulated factors actively inhibit host complement to facilitate aggregation. Taken together, these data suggest that the formation of immune-tolerant biofilm aggregates may contribute to chronic device related infections by protecting bacteria from phagocyte killing. These studies provide vital insight into the host pathogen interactions on contaminated biomaterial surfaces and highlight early events that may determine infection outcome.