2018 Irving H. Wiesenfeld Fellow

Nora Kostow

UC Berkeley PhD Candidate in Molecular & Cell Biology Department, Welch Lab

Nora Kostow is a PhD candidate in the Molecular and Cell Biology program at UC Berkeley. She obtained her BA from Grinnell College in 2013 with a major in biology. She moved to Berkeley in 2013 to work in the Dernburg lab and joined the PhD program in 2016. For her thesis work. She joined the lab of Dr. Matthew Welch where she studies host-pathogen interactions during cell-to-cell spread. Her research focuses on how the bacterium *Burkholderia thailandensis* spreads by inducing cell-cell fusion.

Fellowship Proposal

Burkholderia pseudomallei is a Gram-negative, facultative, cytosolic bacterial pathogen that is the causative agent of melioidosis in humans, an often-fatal disease prevalent in Southeast Asia and northern Australia. *B. pseudomallei* and related species are the only bacterial pathogens known to spread by inducing cell-cell fusion of host cells, however, little is known about the mechanism of *B.thailandensis* induced cell-cell fusion aside from the requirement of two major features. First, intracellular motility of *B. thailandensis* is thought to bring the plasma membrane of neighboring cells into proximity, which is required for membrane fusion in general. The second required feature is the fifth type 6 secretion system (T6SS-5) and its tip protein VgrG-5.mUnderstanding the mechanism of cell-cell fusion will elucidate a key aspect of *Burkholderia* pathogenesis, which may impact our understanding of how to combat melioidosis.

Nora hypothesizes that *B. thailandensis* induces cell-cell fusion through a series of steps including membrane protrusion formation and membrane fusion pore formation, of which the VgrG-5 functions as the plasma membrane fusogen during this process. The aims of Nora's project will be to visualize *B. thailandensis* cell-cell fusion using live cell microscopy using GFP-labeled bacteria to infect A549 (human lung epithelial) cells expressing an RFP-tagged farnesyl plasma membrane marker, followed by characterization of VgrG-5 function in cell-cell fusion.

The results of Nora's studies will reveal when and where protrusion formation and membrane fusion occur, as well as have the potential to uncover alternative approaches to inhibit growth of this antibiotic-resistant pathogen in vivo, for example by inhibiting VgrG-5-mediated cell-cell fusion. In addition, this investigation into understanding how *Burkholderia spp.* spread from cell-to-cell will help illucidate the mechanisms used by these pathogens for virulence. Research into their pathogenicity and spread will help in developing new strategies for targeting them.