

MORGAN RICE¹, NOAH TEAFF¹, DONALD PRIMERANO², JAMES DENVIR², and DEANNA M. SCHMITT¹. ¹Department of Natural Sciences and Mathematics, West Liberty University, West Liberty, WV, 26074. ²Genomics and Bioinformatics Core Facility, Marshall University, Huntington, WV, 25755. Role of Francisella lipoprotein A (FlpA) in Francisella tularensis susceptibility to resazomycins

Francisella tularensis is classified by the CDC as a Category A bioterrorism agent because of its ease of aerosolization, low infection dose, and high mortality rate. Inhalation of as few as one bacterium is sufficient to cause an acute pneumonia that is lethal in up to 60% of individuals if left untreated. Therefore, the intentional release of antibiotic-resistant strains of *F. tularensis* would be disastrous and new therapeutics targeting this bacterium must be developed to make our nation safer against a potential terror attack. We have identified a family of resazurin-based compounds called resazomycins that exhibit robust antimicrobial activity against select Gram-negative bacteria, including *F. tularensis*. The mechanism of action of these antibiotics is not known. To identify potential targets of resazomycins, we performed a high throughput screen to identify resistant isolates and then performed whole genome sequencing on each isolate. Multiple *F. tularensis* isolates had a mutation in the gene FTL_0073 which encodes for *Francisella* lipoprotein A (FlpA). Based on the localization of FlpA to the outer membrane, we hypothesize that this protein could be a target of resazomycins or may play a role in uptake of this antibiotic. To address these two hypotheses, we are currently working to generate a *flpA* disruption and null deletion mutant using standard molecular genetic techniques. Once the mutants are generated, we will first confirm the sensitivity of the *flpA* mutants to resazomycins. Then, we will test the mutant for defects in uptake of resazomycins. Understanding the role of *flpA* in resazomycin susceptibility would facilitate further development of these compounds as potential treatments for tularemia.