Investigator:	**Philip Rather** Phone: (404) 728-5079 Email: prather@emory.edu
Primary Research Interest:	Microbiology
Description of Research:	Research in the Rather laboratory focuses on the bacterium Acinetobacter baumannii, a critical threat to hospitalized patients and injured military personnel. We have identified a genetic switch that allows A. baumannii to interconvert between virulent and avirulent states. By manipulating this switch, a strain has been created that is locked in the avirulent state. Our studies have demonstrated that this locked strain serves as a highly effective live attenuated vaccine and confers 100% protection in mouse models of infection. In addition, high-throughput screening is being used to identify small molecules that convert A. baumannii from the virulent to the avirulent state. The overall goal of our work is to develop both a vaccine and novel antimicrobials to target this highly antibiotic resistant pathogen. In a second are of research, we are studying the effects of beta-lactamase overexpression on the physiology of A. baumannii. Our work has demonstrated that beta-lactamase overexpression can create new cellular vulnerabilities in A. baumannii, and genes that have a synthetic lethal phenotype in overexpressing strains have been identified. These gene products represent a new class of bacterial targets for the development of novel antimicrobials that selectively target antibiotic resistant bacteria.
Relevance to VA:	Acinetobacter baumannii has become a critical pathogen in U.S. hospitals, including those in the VA Healthcare system. A. baumannii is responsible for approximately 2 million infections and 450,000 deaths annually worldwide. Since 2008, there have been approximately 5,000 infections due to A. baumannii in VA hospitals nationwide, with a mortality rate of 28%. In addition, A. baumannii has been responsible for the majority of infections in military personnel injured in combat. In particular, deep soft tissue and orthopedic infections were commonly seen, with extremities the most frequent site of infection. Due to the rapidly growing problem of antibiotic resistance in A. baumannii, where untreatable infections are a reality, new drug discovery approaches are critically needed. Our lab has identified a novel regulatory mechanism that controls the interconversion between virulent and avirulent forms of A. baumannii. This pathway represents an “Achilles-heel” for A. baumannii, as methods to convert virulent opaque to avirulent translucent cells or lock cells in the avirulent translucent state would render cells avirulent. Importantly, our previous work in understanding the control of this virulence switch has led to the creation of a strain genetically locked in the avirulent state, which serves as a highly effective live attenuated vaccine with 100% protection in animal models.