University of South Florida

The Department of Cell Biology, Microbiology and Molecular Biology

Announces a seminar by

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"Exploring the Proteinaceous Regulome of *Acinetobacter baumannii*"

Acinetobacter baumannii infections are commonly associated with life threating and deadly infections in patients from healthcare facilities. Approximately, 60% of *A. baumannii* infections in the United States are caused by multidrug resistant strains with mortality rates between 50% to 60% in patients with ventilator associated pneumonia and bacteremia. Consequently, the Worldwide Health Organization has categorized *A. baumannii* as a critical pathogen for which current antimicrobial treatments are essentially non-existent. As a result, there is a desperate and urgent need for new knowledge regarding pathogenic and drug resistance mechanisms in this organism. Notably, there are a wealth of reports describing virulence factors and genes contributing to these processes, however little is known about the regulatory network controlling their expression. Therefore, we performed an extensive bioinformatics analysis that identified regulatory proteins in the clinically relevant strain AB5075. This work identified a core regulome of 243 transcription factors, 14 two-component systems and 5 sigma factors. Experimental analysis of the 9 uncharacterized TCSs identified a response regulator (RR) mutant and its corresponding sensor kinase as having increased susceptibility to aminoglycosides. Further study revealed that this observation is driven by alterations in membrane energy homeostasis, which leads to decreased efflux pumps activity, membrane depolarization, decreased intracellular pH, decreased survival in blood and attenuated virulence in a murine pneumonia model. Transcriptional analysis using a reporter gene fusion revealed that expression of this TCS was induced in the presence of the protonophore carbonyl cyanide m-chlorophenylhydrazone (CCCP) supporting a role in maintaining membrane energetics. In addition to this TCS, we are currently investigating the potential role of the putative ECF-sigma factor, FecI, in hemin uptake. Specifically, we observed that disruption of the *fecI* gene resulted in growth inhibition under hemin limited conditions with is in line with a potential role of *fecI* in activation of hemin uptake. Further work will elucidate the regulatory role of *fecI* hemin acquisition. Collectively, these studies provide a deeper understanding of the role of regulatory proteins in *A. baumannii* and their contribution to intrinsic multidrug-resistance and virulence-related phenotypes in this pathogen.

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