RUTGERS
School of Graduate Studies

Office of Student Affairs and Admissions
SGS at New Jersey Medical School
Rutgers, The State University of New Jersey
185 South Orange Avenue, MSB C-696
Newark, NJ 07103

http://njms.rutgers.edu/gsbs/
p. 973-972-4511
f. 973-972-7148

YOU ARE INVITED TO ATTEND THE DEFENSE OF THE DOCTORAL DISSERTATION

"Molecular Analysis of *Aggregatibacter Actinomycetemcomitans*, ApiA and its Influence on Factor H."

by

Sera T. Jacob

Cell Biology, Neuroscience and Physiology Program

BS Biotechnology, Bishop Moore College, Kerala University, India
MS Biotechnology, Sri Ramachandra Medical College, Chennai, India

Thesis Advisor:

Dr. Daniel H. Fine
Department of Oral Biology

Thursday, June 2nd, 2022
1.00 P.M.
RSDM C830

https://rutgers.webex.com/rutgers/j.php?MTID=mc9eddab8fff1bf65506ca7e918b895fd
Meeting ID: 2624 822 9718
Password: aCAFyYub744

ABSTRACT

Aggregatibacter actinomycetemcomitans (*Aa*), a Gram-negative oral bacterium, is strongly associated with Localized Aggressive Periodontitis (LAP). *Aa* binds to (BECs) to initially colonize and then lead to disease progression or infection. Various *Aa* virulence traits are essential for the LAP progression and the genes associated with virulence are expressed and regulated in a timely manner, depending on the different environmental conditions that the organism is exposed to for successful colonization. This mechanism of initial colonization by adherence is likely through the outer membrane proteins of the bacterium. ApiA (Actinobacillus Putative Invasin) is a trimeric autotransporter outer membrane and a major immunodominant multi-functional protein that facilitates binding of *Aa* to (BECs) in the oral cavity. *Aa* actively senses and responds to serum, subverting the first-line innate immune defense of complement-mediated killing that is encountered in the gingival crevice, therefore rendering the bacterium resistant to the cytotoxic effects by various of its virulence factors. This sensing or detection by ApiA facilitates microbial and mammalian cell interactions by binding to buccal epithelial cells for its initial colonization, also promotes bacterial serum resistance by binding and sequestering of complement FH, a major regulator of the alternative complement system, thus acting as an immune modulator.

Aa is an extremely complex organism that expresses multiple virulence factors on its surface. So, in order to study ApiA isolated from these other outer membrane proteins, the study was designed to use E. *coli* as a neutral host. Using this model, we could create a series of gene deletions for identification of a region most responsible for surface expression of genes related to serum resistance. Surface expression of ApiA was confirmed by functional assays that included both autoaggregation, and epithelial binding assays. Our experiments, using the *E. coli* host were the first to demonstrate the specific region that's critical in conferring serum resistance and in the identification of the region within ApiA passenger domain that's responsible for binding Factor H. Our efforts to demonstrate the relationship of ApiA to serum resistance in *Aa* showed that other genes or regulatory factors must prevail because knocking out ApiA only resulted in a 25 % reduction in serum resistance. Efforts to identify other likely genes related to serum resistance failed to demonstrate modulation when ApiA deletions were exposed to serum using qPCR. We will use RNA seq to identify alternative ways in which *Aa* can respond to a challenge from serum.

It is clear that serum resistance in *Aa* is an important virulence trait because several genes appear to be required. Factor H and serum resistance appear to be important elements in *Aa* survival in the early stages of disease. Understanding bacterial/host interactions through Factor H can provide insight into how to combat disease by developing therapeutic strategies. Factor H biology can help define the molecular communication between *Aa* and host cells in disease homeostasis and dysbiosis.