

M & I
Microbiology
and Immunology
University of North Carolina at Chapel Hill

DISSERTATION SEMINAR

Josh Quinn

“Temperature and pH regulate PsaE and PsaF to control expression of *psaA* in *Yersinia pestis*.”

Friday, February 14, 2020
3:30 p.m.

Medical Biomolecular Research Building (MBRB) G-202

Dissertation Advisor: Dr. Virginia Miller

Presented in partial fulfillment of the requirements for the degree of Doctor of
Philosophy

ABSTRACT

Josh Quinn: Temperature and pH regulate PsaE and PsaF to control expression of *psaA* in *Yersinia pestis*
(Under the direction of Virginia Miller)

Yersinia pestis is a Gram-negative bacterial pathogen that causes the disease plague. Plague is a fulminant disease with a high mortality rate if left untreated, leading *Y. pestis* to be one of the deadliest pathogens in human history. Bubonic plague is the most common form of the disease in humans and many bacterial factors important for disease are poorly understood.

The *Y. pestis* “pH 6 antigen” (PsaA) forms fimbriae and is important for bubonic plague pathogenesis. The combination of high temperature and low pH induces PsaA production and while the influence of these environmental cues on the production of PsaA is evident, the molecular mechanisms underlying this unusual regulation are not defined. Little attention has been focused on the regulation of *psaA* in *Y. pestis* and much of our current knowledge is based upon studies of *psa* in *Y. pseudotuberculosis* and the orthologous system, *myf*, in *Y. enterocolitica*. The focus of this dissertation was to characterize mechanisms *Y. pestis* utilizes to control *psaA* expression. Using defined growth conditions, we determined that *psaA* expression in *Y. pestis* is induced in response to high temperature and low pH and this requires two genes, *psaE* and *psaF*, located directly upstream of *psaA*. We generated antibodies that recognize endogenous PsaE and PsaF and showed that temperature and pH regulate the levels of these proteins. High temperature is required for the translation of *psaE* and *psaF* and thus controls the production of PsaE and PsaF. Additionally, we identified a distinct pH threshold that defines PsaE and PsaF levels. PsaE and PsaF exhibit co-dependent stability and we identified residues in the periplasmic domains of each protein that enhance their stability. Histidine residues in the periplasmic domain of PsaF sense pH and thus, through its influence on PsaE stability, PsaF appears to function as a pH sensor that controls *psaA* expression.

Together, our data indicate that *Y. pestis* utilizes temperature and pH to regulate the levels of PsaE and PsaF and precisely coordinate *psaA* expression. This work contributes to the understanding of molecular mechanisms that bacteria utilize to sense environmental variations and control gene expression.