

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

## THESIS SEMINAR

**Zach Nash**

**“Grab and Stab: Cooperation between an adhesin  
and a toxin for a cell-specific weapon delivery  
system in *Bordetella*.”**

Thursday, December 12, 2019  
3:30 p.m.  
1131 Bioinformatics

Thesis Advisor: Dr. Peggy Cotter

Presented in partial fulfillment of the requirements for the degree of  
Master of Science

## ABSTRACT

**Zach Nash:** Grab and Stab: Cooperation between an adhesin and a toxin for a cell-specific weapon delivery system in *Bordetella*  
(Under the direction of Peggy Cotter)

Pertussis, also known as whooping cough, is a human respiratory illness caused by the Gram-negative bacterium *Bordetella pertussis*. The critically important *Bordetella* virulence factor filamentous hemagglutinin functions in adhesion and immunomodulation and is both membrane bound and released from the bacterium. It is also a prototypical member of the widespread Two Partner Secretion pathway family of proteins. Filamentous hemagglutinin is synthesized as the 370 kDa protein FhaB, which possesses a large C-terminal “prodomain” that is eventually degraded in a regulated manner to create the 260 kDa protein FHA. The full length protein and proper degradation of the prodomain are necessary for bacterial persistence in the host, yet little is known about the degradation mechanism and function. We have identified CtpA as a periplasmic protease responsible for prodomain degradation and have shown that stepwise proteolysis by CtpA, the autotransporter protease SphB1, and a yet unidentified protease is required for conversion of FhaB into FHA, release of FHA into extracellular milieu, and full protein function *in vivo*. We also present evidence supporting the hypothesis that degradation occurs to facilitate cell-specific delivery of adenylate cyclase toxin to phagocytes. These data support a substantially updated model for the mechanism of secretion, maturation, and function of this model Two Partner Secretion protein.