

## ABSTRACT

Tick-borne tularemia was first described in 1924. Nearly 100 years later, questions remain about the tick vector(s) that pose(s) the greatest risk for transmitting *Francisella tularensis* (*Ft*), the causative agent of tularemia. Additionally, few studies have identified genes/proteins required for *Ft* to infect, persist, and replicate in ticks. To answer questions about vector competence and *Ft* transmission by ticks, we infected *Dermacentor variabilis* (*Dv*), *Amblyomma americanum* (*Aa*), and *Haemaphysalis longicornis* (*Hl*; invasive species from Asia) ticks with *Ft*, finding that although *Aa* ticks initially become infected with 1-log higher *Ft*, *Ft* replicated more robustly in *Dv* ticks, and did not persist in *Hl* ticks. In transmission studies, both *Dv* and *Aa* ticks efficiently infected naïve mice, causing disease in 57% and 46% of those mice, respectively. We identified a putative *Ft* chitinase, *FTL1793*, generated a  $\Delta$ *FTL1793* mutant, and found that  $\Delta$ *FTL1793* was deficient in tick infection, persistence, and replication in ticks. Recombinant *FTL1793* exhibited chitinase activity *in vitro*, suggesting that this chitinase may provide an alternative energy source for *Ft* in ticks. Taken together, *Dv* ticks appear to pose a greater risk for harboring and transmitting tularemia and *FTL1793* plays a major role in promoting tick infections by *Ft*.



COLLEGE OF MEDICINE  
AND LIFE SCIENCES

THE UNIVERSITY OF TOLEDO

## THESIS COMMITTEE

Jason Huntley, Ph.D. (Mentor)  
R. Mark Wooten, Ph.D.  
Randall Worth, Ph.D.

Medical Microbiology and  
Immunology (MMI) Track

Department of Medical  
Microbiology & Immunology



THE UNIVERSITY OF  
**TOLEDO**  
1872

THESIS  
PRESENTATION

by

**Brenden Tully**  
November 23rd, 2020

*A Francisella tularensis* Chitinase  
Contributes to Bacterial  
Persistence and Replication in  
Two Major U.S. Tick Vectors

M.S. in Biomedical  
Sciences

## PRESENTATIONS AND AWARDS

**Tully, B.G.**, Huntley, J.F. “Infection, Persistence, and Transmission of *Francisella tularensis* in *Dermacentor variabilis* and *Amblyomma americanum*” Poster Presentation at the 26th Midwest Microbial Pathogenesis Conference, Toledo, OH, September 2019.

**Tully, B.G.** “Understanding *Francisella tularensis* Infection, Persistence, and Transmission by Ticks” Graduate Student Association Research Award, University of Toledo, 2020.

## PUBLICATIONS

**Tully, B.G.**, Huntley, J.F. (2020). Mechanisms Affecting the Acquisition, Persistence and Transmission of *Francisella tularensis* in Ticks. *Microorganisms* 8(11): E1639.

**Tully, B.G.**, Huntley, J.F. (2020). A *Francisella tularensis* Chitinase Contributes to Bacterial Persistence and Replication in Two Major U.S. Tick Vectors. *Pathogens*. (under review)

Briana Zellner, Dominique Mengin-Lecreulx, **Brenden Tully**, William T. Gunning 3rd, Robert Booth, Jason F. Huntley (2020). A *Francisella tularensis* L,D-carboxypeptidase plays important roles in cell morphology, envelope integrity, and virulence. *Molecular Microbiol.* (under review)

Adela S. Oliva Chávez, Xiaowei Wang, Liron Marnin, Nathan K. Archer, Holly L. Hammond, Erin E. McClure Carroll, Dana K. Shaw, **Brenden G. Tully**, Amanda D. Buskirk, Shelby L. Ford, L. Rainer Butler, Preeti Shahi, Kateryna Morozova, Cristina C. Clement, Lauren Lawres, Anya J. O’Neal, Choukri Ben Mamoun, Kathleen L. Mason, Brandi E. Hobbs, Glen A. Scoles, Eileen M. Barry, Daniel E. Sonenshine, Utpal Pal, Jesus G. Valenzuela, Marcelo B. Sztein, Marcela F. Pasetti, Michael L. Levin, Michail Kotsyfakis, Steven M. Jay, Jason F. Huntley, Lloyd Miller, Laura Santambrogio, Joao H.F. Pedra (2020). Extracellular Vesicles Act as a Molecular Rheostat Controlling Virulence During Vector Borne Microbial Transmission. *Nature Communications*. (under review)

## FUTURE PLANS

Brenden plans to stay in Toledo, OH to gain skills in healthcare before attending physician assistant school next year.

## ACKNOWLEDGEMENTS

I would like to thank my advisor Dr. Jason Huntley for his guidance throughout my education, including learning many technical, writing, and presentation skills. Additionally, I am thankful for the support of past and present members of the Huntley Lab and MMI department. I would like to thank my committee members Dr. R. Mark Wooten and Dr. Randall Worth for their support and guidance. Finally, I would like to thank my friends and family for their continued presence and support.