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Abstract

"Potentiation of pro-inflammatory responses by a Legionella pneumophila effector in accidental hosts"

Legionella pneumophila (*Lpn*) is an opportunistic human pathogen that is ubiquitous in freshwater environments where it parasitizes and replicates within unicellular protozoa. Colonization of anthropomorphic freshwater environments and subsequent inhalation of aerosolized bacteria can cause a severe pneumonia called Legionnaires' Disease in immunocompromised individuals. Legionnaires' Disease is caused by uncontrolled *Lpn* replication within alveolar macrophages. To replicate within phagocytic cells, *Lpn* relies on a large arsenal of over 300 translocated effector proteins that are delivered directly into host cells by a Dot/Icm type IVB secretion system. *Lpn* is an accidental human pathogen and transmission between humans is very rare. Consequently, *Lpn* has not evolved sophisticated immune evasion strategies and does not cause disease in healthy immunocompetent individuals. Translocated effectors play an important role in clearance of *Lpn* from healthy hosts. Our recent work has revealed that the effector LegC4 is detrimental for *Lpn* replication in the mammalian lung. We found that loss-of-function mutations in the *legC4* gene enable enhanced *Lpn* replication within cytokine activated bone marrow-derived macrophages (BMDMs) and in a mouse model of Legionnaires' Disease. Concomitantly, overexpression of *legC4* attenuates *Lpn* replication in BMDMs.

Thus, LegC4 contributes to *Lpn* clearance from healthy hosts and understanding the mechanism by which this occurs will provide important insights into host defense against bacterial pathogens.

Bio-Summary

Dr. Shames joined the Division of Biology at Kansas State University as an Assistant Professor in October 2017. Dr. Shames earned her Honors Bachelor of Medical Sciences degree in Microbiology and Immunology from the University of Western Ontario (London, Ontario) where she started her research career in Dr. John McCormick's laboratory by investigating mechanisms by which bacterial superantigens interact with T cell receptors. Dr. Shames earned her Ph.D. in Microbiology and Immunology at the University of British Columbia (Vancouver, British Columbia) under the mentorship of Dr. Brett Finlay. While a graduate student in the Finlay lab, Dr. Shames characterized the function of two effector virulence factors from Enteropathogenic *Escherichia coli*. Dr. Shames' post-doctoral training was completed in the Department of Microbial Pathogenesis at Yale University School of Medicine under the supervision of Dr. Craig Roy. During her post-doc, Dr. Shames employed insertion sequencing (INSeq) to identify and characterize virulence factors from the accidental human pathogen, *Legionella pneumophila, in vivo*. Current research in the Shames Lab is focused on using *Legionella* species as model pathogens to reveal molecular mechanisms of innate immunity against intracellular bacterial pathogens.