ABSTRACT

Cholera is a severe intestinal infection characterized by voluminous, watery diarrhea that can be fatal within hours. It is caused by the marine bacterium *Vibrio cholerae* of serogroups O1 and O139. While rare in the United States and other industrialized nations, cholera is endemic in more than 50 countries. In both its aquatic and intestinal life cycles, *V. cholerae* will encounter various stressful conditions, such as fluctuating pH, bacteriophage predation, and exposure to antimicrobial peptides that may negatively affect the integrity of the inner membrane. The phage shock protein (Psp) system is a stress response pathway that senses and responds to such insults. The genetic components of the Psp system are present in several clinically relevant Gram-negative bacteria, including *V. cholerae*. However, most of the current knowledge about the Psp response stems from *in vitro* studies in *Escherichia coli* and *Yersinia enterocolitica*. In fact, the Psp response in *V. cholerae* has remained completely uncharacterized. In this dissertation, it is demonstrated that *V. cholerae* does have a functional Psp response system. The overexpression of GspD (EpsD), the type II secretion system secretin, induces the Psp response, whereas other *V. cholerae* secretins do not. In addition, several environmental conditions were identified as inducers of this stress response. Experiments on the genetic regulation and induction of the Psp system in *V. cholerae* suggest that the key regulatory elements are conserved with those of other Gram-negative bacteria. While a *psp* null strain is fully capable of colonizing the infant mouse intestine, it exhibits a colonization defect in a zebrafish model, indicating that this response may be important for disease transmission in the environment. Overall, these studies provide an initial understanding of a stress response pathway that has not been previously investigated in *V. cholerae*.

COLLEGE OF MEDICINE AND LIFE SCIENCES
THE UNIVERSITY OF TOLEDO

DISSERTATION COMMITTEE

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DISSERTATION PRESENTATION
by

Cara DeAngelis

April 26th, 2019

Characterization of the *Vibrio cholerae* phage shock protein response

Ph.D. in Biomedical Sciences

AWARDS/ LEADERSHIP

2019—Graduate Research Award

2019—College of Business and Innovation Advanced Leadership Academy

2019—Member of the Graduate Student Association Student Insurance Committee on Health

2018-2019—Council of Biomedical Graduate Students President

2017-2018—Council of Biomedical Graduate Students Vice President

2016-2017—Council of Biomedical Graduate Students MMI Representative

2017—Council of Biomedical Graduate Students Graduate Research Forum 3rd place oral presentation

2016– Accepted to Advanced Bacterial Genetics 3 week intensive course at Cold Spring Harbor Laboratory

2016—Helmsley Fellowship for Cold Spring Harbor

2016—Council of Biomedical Graduate Students Graduate Research Forum 3rd place poster presentation

PUBLICATIONS

DeAngelis, C.M., Nag, D., Withey, J.H., and Matson, J.S. Characterization of the *Vibrio cholerae* phage shock protein response. Journal of Bacteriology, 2019. *In Press*.

DeAngelis, C.M., Saul-McBeth, J., and Matson, J.S. *Vibrio responses to extracytoplasmic stress.* Environmental Microbiology Reports, 2018. **10**(5): p. 511-521.

DeAngelis, C.M. 2017. "UT researchers take new approach in cholera prevention." *The Toledo Blade.*

FUTURE PLANS

Cara plans to continue searching for a postdoctoral position and travel internationally for the first time.

PRESENTED ABSTRACTS

DeAngelis, C.M., Nag, D., Withey, J.H., and Matson, J.S "Characterization of the phage shock protein response." Poster Presentation at MMPC, Iowa City, IA, 2018

DeAngelis, C.M., Nag, D., Withey, J.H., and Matson, J.S. "Characterization of the phage shock protein response." Poster Presentation at Midwest Vibrio Summit, Bloomington, IN, 2018

DeAngelis, C.M., Matson, J.S., "Characterization of the phage shock protein response." Poster Presentation at Biomedical Graduate Research Forum**,** Toledo, OH**,** 2018

DeAngelis, C.M., Matson, J.S., "Characterization of the phage shock protein response." Poster Presentation at ASM Conference on Vibrio2017: The Biology of Vibrios, Chicago, IL, 2017

DeAngelis, C.M., Matson, J.S., "Characterization of the phage shock protein response." Oral Presentation at the 8th Annual MGRS, Toledo, OH, 2017

DeAngelis, C.M., Matson, J.S., "Characterization of the phage shock protein response." Oral Presentation**,** GRF, Toledo, OH, 2017

DeAngelis, C.M., Matson, J.S., "Extracytoplasmic stress responses: σ^E and the phage shock protein response." Poster Presentation at MMPC, Urbana-Champaign, IL, 2016

DeAngelis, C.M., Matson, J.S., "Extracytoplasmic stress responses: σ^E and the phage shock protein response." Poster Presentation at the 7th Annual MGRS, Toledo, OH, 2016

DeAngelis, C.M., Matson, J.S., "Extracytoplasmic stress responses: σ^E and the phage shock protein response." Poster Presentation at the GRF, Toledo, OH, 2016