

Characterizing the role of SipA in *Vibrio cholerae*: Investigating the connection between SipA and other aspects of *V. cholerae* physiology

Tanisha Chaudhary¹, Jyl Matson^{2*}

¹College of Medicine and Life Sciences, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

²Associate Professor, Department of Medical Microbiology and Immunology, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

Email: jyl.matson@utoledo.edu

Received: 1/3/2025

Accepted: 2/14/2025

Published: 10/9/2025

Introduction: Stress response mechanisms are crucial for bacterial survival under varying environmental conditions. This study focuses on the highly conserved SipA protein in *Vibrio cholerae*, which is essential for stress tolerance and impacts bacterial physiology, including biofilm formation and carbon utilization. Despite significant preliminary findings, the regulatory mechanisms and functional roles of SipA remain poorly understood.

Methods: In past studies we employed genetic and biochemical approaches, including mutant strain construction, survival and β -galactosidase assays, and advanced techniques like immunoprecipitation and mass spectrometry. Localization studies confirmed SipA's cellular position, while regulatory pathways were investigated through transcriptomic analysis. Both Classical and El Tor biotypes of *V. cholerae* were studied to reveal biotype-specific roles of SipA.

Results: Previous research established that SipA is regulated by a two-component system (VC1638-VC1639), which influences its expression in response to environmental stress, particularly the presence of antimicrobial peptides (AMPs). SipA plays a critical role in AMP resistance by interacting with the outer membrane protein OmpA, suggesting that they work together to facilitate AMP export and alleviate stress. This cooperative mechanism likely involves SipA aiding in the binding or transport of AMPs through OmpA, thereby reducing their toxic accumulation in the periplasm. To better understand how the two proteins relieve AMP stress, we are using *ompA* deletion strains and cellular fractionation assays to assess accumulation of AMPs in the periplasm. Additionally, we have observed that *sipA*-deficient strains exhibited increased biofilm production and growth defects on specific carbon sources, indicating its broader physiological roles beyond stress resistance.

Conclusions: SipA is a multifaceted protein central to *V. cholerae* stress responses and physiology. Its role in AMP resistance highlights a conserved mechanism with potential applications in understanding bacterial stress survival strategies.

Keywords: SipA, OmpA, *Vibrio Cholera*
