

Harmful Algal Bloom Toxin Microcystin-LR Induces Macrophage Inflammation of Lung Tissues

Shivani C. Patel^{1*}, Joshua D. Breidenbach, MS¹, Thomas M. Blomquist¹, Andrew Kleinhenz¹, Apurva Lad¹, Robin C. Su, PhD¹, Benjamin W. French¹, Shereen G. Yassine¹, James C. Willey, MD², Jeffrey R. Hammersley, MD¹, Amira Gohara, MD³, R. Mark Wooten, PhD⁴, Erin Crawford, Nikolai Modyanov⁵, MD, Deepak Malhotra, MD⁶, Steven T. Haller, PhD¹, David J. Kennedy, PhD¹

¹Division of Cardiology, Department of Medicine, The University of Toledo, Toledo, OH 43614

²Division of Pulmonology and Critical Care, Department of Medicine, The University of Toledo, Toledo, OH 43614

³Division of Pathology, Department of Medicine, The University of Toledo, Toledo, OH 43614

⁴Department of Physiology and Pharmacology, The University of Toledo, Toledo OH 43614

⁵Division of Infectious Diseases, The University of Toledo, Toledo, OH 43614

⁶Division of Nephrology, The University of Toledo, Toledo, OH 43614

*Corresponding author: Shivani.Patel8@rockets.utoledo.edu

Published: 05 May 2023

Introduction: Harmful Algal Blooms, or HABs, are rapidly growing algae or cyanobacteria that may produce toxins, which are dangerous for humans and animals. They arise from warm temperatures and nutrient pollution. HAB toxins, such as Microcystin-LR (MC-LR) present public health concerns, such as the transmission of HAB toxins via the generation of aerosols. Exposure to aerosolized HAB toxins may even potentially be linked to hazardous health consequences, such as airway inflammation. In previous studies, oral exposure to MC-LR in rodents led to macrophage infiltration of the colon. Therefore, the objective of this study was to investigate the role of macrophages in the airways in response to MC-LR exposure.

Methods: C57BL/6J and BALB/c mice were exposed to MC-LR aerosols at a concentration designed to mimic potential environmental exposure. Lung tissues were analyzed for exposure dependent changes in gene expression, cytokine concentrations, and immune cell infiltration.

Results: Gene expression profiles of mice exposed to HAB toxin aerosols demonstrated a significant increase in the CD68 gene expressed by macrophages in C57BL/6J mice. Cytokine and chemokine protein concentration profiles also showed significant increases in multiple macrophage associated

markers. Furthermore, IHC stains of lung tissue also revealed higher numbers of macrophages in C57BL/6J, but not BALB/c mice.

Conclusion: It appears that airways exposed to MC-LR aerosols respond with an increase in macrophage inflammation. These findings warrant further investigation into the impact of this toxin in populations with pre-existing airway inflammation.