Aerosolized Harmful Algal Bloom Toxin Microcystin-LR Induces Inflammatory Signaling in Human Airway Epithelial Cells

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Introduction: Harmful algal blooms plague bodies of freshwater globally. These blooms are often composed of outgrowths of cyanobacteria capable of producing the heptapeptide Microcystin-LR (MC-LR) which is a well-known hepatotoxin. Recently, MC-LR has been detected in aerosols generated from lake water. However, the risk for human health effects due to MC-LR inhalation exposure have not been extensively investigated.

Methods: In this study, we exposed a fully differentiated 3D human airway epithelium derived from 14 healthy donors to MC-LR-containing aerosol for 3 minutes per day for 3 days. Concentrations of MC-LR ranged from 100 pM to 1 μM.

Results: Although there were little to no detrimental alterations in measures of the airway epithelial function (i.e. cell survival, tissue integrity, mucociliary clearance, or cilia beating frequency), a distinct shift in the transcriptional activity was found. Genes related to inflammation were found to be upregulated such as C-C motif chemokine 5 (CCL5; log2FC = 0.56 , p = 0.02) and C-C chemokine receptor type 7 (CCR7; log2FC = 0.83, p = 0.03). Functionally, conditioned media from MC-LR exposed airway epithelium was also found to have significant chemo-attractive properties for primary

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human neutrophils. Additionally, increases were found in the concentration of secreted chemokine proteins in the conditioned media such as CCL1 (log2FC = 5.07 , p = 0.0001) and CCL5 (log2FC = 1.02, p = 0.046).

Conclusion: These results suggest that MC-LR exposure to the human airway epithelium is capable of inducing an inflammatory response that may potentiate acute or chronic disease.

