Exposure to Microcystin-LR Induces Differential Gene Regulation in Primary Human Keratinocytes

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Introduction: Harmful algal blooms (HABs) are on the rise globally, including in Lake Erie near Toledo. HABs are composed of blue-green algae, or cyanobacteria, which produce cyanotoxins, like microcystins, anatoxins, and saxitoxins, among others. Over 270 congeners of microcystin exist, but microcystin-LR (MC-LR) is most prevalent and potent. Dermal contact represents one of the most common exposure routes to MC-LR and dermal lesions account for a significant majority of HAB exposure symptoms. Despite this, almost no work has been published on the toxicity of microcystins in the skin.

Objectives: Determine potential health impacts in human keratinocytes after exposure to MC-LR, looking at inflammatory markers and structural barrier proteins

Methods: Primary keratinocytes were cultured in 12 well-plates and exposed to 1 or 10 µM MC-LR for 6, 12, and 24 hours (n=3/group). After the exposure periods, cells were subjected to RT-PCR, assessing inflammatory markers and key structural barrier proteins.

Results: 1 µM MC-LR exposure caused a time-dependent increase in the expression of structural barrier proteins involucrin (IVL), loricrin (LOR), and filaggrin (FLG), with this trend reaching significance at 24 hours post-exposure (IVL p = 0.0007; LOR p = 0.0276; FLG p < 0.0001). Similarly, the 10 µM MC-LR exposure induced a stepwise increase in the expression of interleukin 1-beta (IL-1B), with significance increases at 12 (p = 0.0138) and 24 hours (p = 0.001). The 10 µM exposure additionally caused an initial spike in Tumor Necrosis Factor α expression at 6 hours (p = 0.0286), followed by a decrease in expression at 24 hours (p = 0.0072).

Conclusions: Our results suggest that MC-LR exposure induces significant activation of key proteins involved in inflammation and the structural integrity of primary human keratinocytes. These findings suggest that microcystins are capable of inducing inflammation in underlying skin lesion phenotypes associated with dermal HAB exposure.