Cyanotoxin Degrading Lake Bacteria Significantly Alleviate Microcystin-LR Induced Hepatotoxicity in Both In Vitro and In Vivo Models

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Introduction: Harmful algal blooms are a potential threat to human health due to the release of cyanotoxins. Our recent reports have shown that exposure to the prevalent cyanotoxin microcystin-LR (MC-LR) exacerbates development of pre-existing liver disease as well as alters gut microbiota that may significantly impact development of hepatotoxicity. We have isolated naturally occurring novel MC-LR degrading bacteria from Lake Erie, OH and hypothesize that they may alleviate MC-LR toxicity.

Methods: Human Hep3B hepatocytes were treated with various ratios of hepatocyte:bacterial cells – 1:10, 1:50 and 1:100 for 30 min. prior to exposure with 10 µM MC-LR. After 24 hrs, cells and supernatants were collected for qPCR and mass spectrometric analysis. Age-matched Balb/c female mice were either given normal or a mix of MC-degrading bacteria (105 CFU/ml) in drinking water for four weeks followed by a single gavage with vehicle or 500 µg/kg of MC-LR and then euthanized 2 or 24 hrs post-exposure. Urine and organs were collected for qPCR and mass spectrometric analysis.

Results: Genetic analysis for markers of hepatotoxicity and inflammation in both in vivo and in vitro settings were significantly downregulated in the presence of MC-degrading bacteria compared to the untreated groups. Mass spectrometric analysis of urine from mice pre-treated with the bacteria prior to MC-LR exposure, revealed significant reduction in urine MC-LR levels and elevated levels of the detoxified metabolite - MC-LR Cysteine as compared to the untreated control group.

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Conclusion: These results suggest a potential novel therapeutic approach that can be developed for MC-LR induced toxicity.

