Differential Expression of Organic Anion Transporting Polypeptides in the Liver and Common Comorbidities: Implication for Toxicity of Microcystins and other Xenobiotics

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Background: Organic Anion Transporting Polypeptides (OATPs) are a family of transporters found throughout the body and encoded by Solute Carrier Organic Anion Transporter (SLCO) genes. The role of OATP in the transport of xenobiotics has gained increased attention due to harmful algal blooms (HABs) and the subsequent release of cyanotoxins like Microcystin-LR (MC-LR) that can harm humans. Exposure is known to cause acute illness including liver injury, however the extent of illness and susceptibility of individuals with common liver disease comorbidities is unknown.

Objectives: We used a differential expression analysis to determine levels of SLCO expression in both healthy individuals and those with common pre-existing liver diseases to understand how hepatic comorbidities may impact susceptibility to HAB cyanotoxin exposures.

Methods: We examined RNA expression levels of OATP related SLCO genes in hepatic tissue across a variety of comorbidities. Differential gene expression data was obtained from the National Center for Biotechnology Information (NCBI), Gene Expression Omnibus (GEO). Search queries in the GEO browser were formatted as “(Disease) AND tissue.” Datasets which did not fulfill “disease vs. healthy” criteria were omitted. Differential Expression Analysis was performed using NCBI’s integrated GEO2R software.

Results: Liver tissue exhibited high expression levels of several SLCO isoforms. When compared to non-diseased control liver samples, SLCO expression was decreased in cirrhotic liver, while liver samples obtained from hyperglycemic and diabetic patients as well as patients with...
hepatocellular carcinoma demonstrated increased expression of SLCO compared with non-diseased controls.

**Conclusion:** This data supports the hypothesis that disease states impact the expression level of SLCOs. Decreased expression in cirrhosis suggests a downregulation of OATP as a response to damaged hepatic tissue. Increased expression in hyperglycemic, diabetic, and hepatocellular carcinoma patients aligns with previous studies from our lab and others indicating that these disease states confer increased susceptibility to cyanotoxin exposure.