

Differential Expression of Organic Anion Transporting Polypeptides in the Kidney: Implication for Cyanotoxins Toxicity

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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's has gained increased attention due to harmful algal blooms (HABs). We have previously demonstrated the kidney is a major target organ of HAB cyanotoxins, however the impact of common kidney comorbidities on OATP transporters 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 kidney disease to understand how renal comorbidities may impact susceptibility to HAB cyanotoxin exposures.

Methods: We examined expression levels of OATP related SLCO genes in renal tissue from 230 participants across a variety of comorbidities. Differential gene expression data was obtained and analyzed through 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.

Results: Renal tissue exhibited a similar pattern of expression of SLCO isoforms to other major organs with the highest level of expression for SLCO isoforms 2A1, 2B1, and 4C1. When compared to non-diseased controls, patients with diabetic nephropathy demonstrated significant ($p < 0.01$) increases in glomerular expression of SLCO isoforms 1B1, 2B1, and 4C1 as well as tubulointerstitial increases in expression of SLCO3A1. There was also mild downregulation of SLCOs 1A2, 1C1, 2B1, and 5A1.

Conclusion: This data supports the hypothesis that disease states impact the expression level of key transporters for cyanotoxins in the kidney. Increased expression in both the glomerular and tubulointerstitial expression of OATP transporters in patients with diabetic nephropathy agrees with experimental evidence suggesting an increased susceptibility to renal injury after cyanotoxin exposure in diabetic models.