OXLATE INDUCED CHANGES IN GENE EXPRESSION IN HUMAN RENAL EPITHELIAL CELLS: IDENTIFICATION OF GENES INDUCED BY OXALATE.

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Kidney stones effect about 10 % of US population and have an economic impact of 2-4 billion US$ annually. The majority (~80 percent) of kidney stones are composed of calcium oxalate crystals. Increased urinary oxalate is an established risk factor for nephrolithiasis. Our laboratory was the first to demonstrate that oxalate is nephrotoxic, and oxalate interactions with the renal cells results in a plethora of changes, including cell growth, death and altered gene expression. Recently we evaluated oxalate induced global changes in gene expression in the renal epithelial (HK2) cells by DNA micro-array chip that represented 11 independent replicate probe sets for each message. These studies identified several genes whose expression was either up or down regulated by oxalate. In the present study the most strongly up and down-regulated genes were confirmed using polymerase chain reaction (PCR) in new experiments, where renal epithelial cells (HK2) were exposed to oxalate. We also extended our studies to define time course (1h-24 h) of gene expression changes upon oxalate exposure. Results of our current studies confirmed that oxalate induced time dependent expression of the beta-adrenergic receptor, beta subunit of the IL-2 receptor, and the transcript of a protein whose function is currently unknown. These exciting observations suggest oxalate may regulate its actions by turning on additional (previously unknown) intracellular pathways that may be involved in stone pathogenesis. Additional studies into these pathways may provide the key to unlocking a biochemical target in stone disease, and are currently underway in our laboratory.