Discovering and Validating New Biomarkers for Drug-Induced Kidney Toxicity in Cancer Patients

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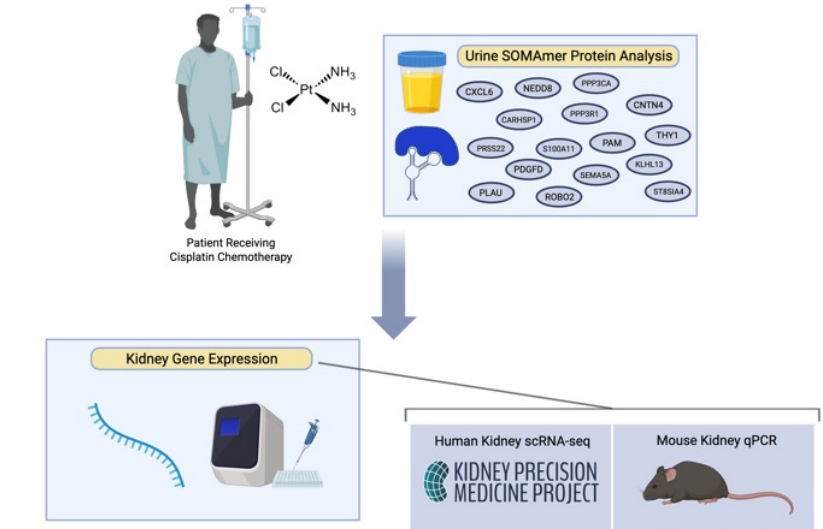
Cisplatin is a chemotherapeutic drug used in the treatment of many solid tumors, but its clinical utility is limited by nephrotoxicity. Current methods of detecting cisplatin-induced acute kidney injury (AKI) are only effective when a significant amount of kidney damage has already occurred. To identify more sensitive novel biomarkers for cisplatin-induced AKI, an untargeted, SOMAmer-based proteomic analysis was conducted on urine samples from 20 patients before and 48 hours after cisplatin treatment. The purpose of this study was to prioritize 53 potential biomarkers for validation using: 1) the human AKI dataset in the Kidney Tissue Atlas and 2) kidneys of mice treated with cisplatin. Total RNA was extracted from frozen kidneys of saline-treated control mice (n=4) and cisplatin (20 mg/kg, ip)-treated mice (n=8) at 72 hrs. cDNA was generated and qPCR was performed for 16 genes. Cisplatin treatment produced kidney mRNA expression changes in 7/16 genes, with 5/16 going in the same direction as the Kidney Tissue Atlas data. One of these 5 genes, Cxcl5, the mouse ortholog of human CXCL6, exhibited an 80-fold increase. This data can be utilized in further validating these identified potential biomarkers of interest in larger sample sizes of patient urine using additional protein assay techniques. Supported by NIH R25ES020721 and the American Society for Pharmacology and Experimental Therapeutics.



Gene Name	Function	Expression Change	Expression Change
Cxcl5	Immunity/chemokine	↑	↑
Carhsp1	RNA-binding	↑	↑
S100a11	Growth/differentiation	↑	↑
Prss22	Serine protease	↑	↑
Klhl13	Protein breakdown	↑	↓
St8sia4	Cell-Cell interaction	↑	↓
Thy1	Cell adhesion	↓	↓