Identification of a Novel Signaling Platform as a Cisplatin Target in Kidney Injury

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Cisplatin is an effective standard of care chemotherapeutic agent used in the clinic for treating a wide range of human tumors. However, kidney injury is an adverse side effect of cisplatin therapy for which treatment is unavailable due to lack of mechanistic understanding of cisplatin action. While cisplatin interferes with DNA replication in highly proliferation tumor cells, it is unknown how it affects normal kidney cells. Our cell biological analyses in cultured cells and animal models largely supported our novel hypothesis that cisplatin targets adhesion proteins in kidney epithelia, disrupts cell-cell contacts and ultimately leads to kidney damage. Here, we provide further supportive evidence from bioinformatics analyses, using the Nephroseq platform. Our RNAseq data analyses identified a distinct signal transduction and structural pathway composed of a receptor tyrosine kinase, a scaffold signal modulator and a group of cell adhesion proteins. Together, these proteins form a signaling platform that regulate secretion and ion transport across kidney tubules. These findings pave the way for devising targeted therapies for cisplatin-induced kidney damage while preserving its efficacy in oncology.

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