An Integrative View of Cisplatin Uptake by Kidney and Renal Toxicity

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Cisplatin (cis-diamminedichloroplatinum II) (CDDP) is an inorganic platinum-based chemotherapeutic agent that is widely used in the treatment of a variety of solid organ cancers. The main dose limiting side effect of CDDP is nephrotoxicity; after a single dose of CDDP (50-100 mg/m²), approximately one-third of the patients develop nephrotoxicity. Yet, in spite of intense therapeutic response to drugs, Drug transporters regulate absorption, distribution and metabolism as well as drugs excretion because of their influence on the OCT1/2 (−/−) mice conferred complete protection [13].

Organic anion transporter 1 (OAT1) (Figure 1B) and OAT3 (Figure 1C) in the kidney proximal tubules and play important roles in the elimination of harmful endogenous compounds and xenobiotics from the body.

Figure 1: 2D structure of (A) hOCT2 (residue range: 126-499). (B) hOAT1 (residue range: 121-515). (C) hOAT3 (residue range: 121-407).

Recently, work by Hu et al. revealed that OAT1/OAT3 is a novel metabolite a mercapturic acid CDDP uptake pathway independent of the OCT2 pathway of CDDP nephrotoxicity and that act upstream of p53 [14]. Collectively, OCT2, OAT1 and OAT3 are critical transporters in CDDP-induced kidney injury. Moreover, further work on the regulation of these transporters could add novel candidate compounds to improve the current state of CDDP therapeutics and offer more alternatives choice for clinicians and patients to promote longer survival and better quality of life.
References