Cisplatin-induced nephrotoxicity

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Nephrotoxicity represents one of the cutting-edge topics of our journal (Francescato et al. 2011; Stewart et al. 2011a, b; Faiz et al. 2011; Briguori et al. 2011; Song et al. 2011; Abdel-Bakky et al. 2011; Liu et al. 2011; Chattopadhyay et al. 2011). Therefore, the editors are pleased that Antonio C. Santos and colleagues from the University of Sao Paulo in Brazil accepted our invitation of a state of the art review on cisplatin-induced nephrotoxicity and strategies of nephroprotection (Santos et al. 2012; this issue). Cisplatin was accidentally discovered by Barnett Rosenberg who initially intended to kill bacteria by an electric field. Later, Rosenberg recognized that cells were not killed by the electric field but by a compound released from the platinum electrodes. Interestingly, cisplatin is cytotoxic via its aquated metabolite. In blood, where chloride concentrations are relatively high, cisplatin remains unaltered. However, as soon as cisplatin enters the cell, it undergoes hydrolysis because of low intracellular chloride concentrations, and the two chloride ions are replaced by water. This aquated form binds to N7 positions of guanine and forms the intrastrand crosslinks representing the cytotoxic mechanism of cisplatin. Besides its DNA binding effect, cisplatin also causes mitochondrial damage leading to reactive oxygen species. Generation of oxidative stress together with relatively high concentrations in the renal transport system explains the preferential kidney toxicity of cisplatin. The authors give a comprehensive overview of the molecular mechanisms of cisplatin-induced toxicity in the kidney and also present the

most efficient clinical strategies to prevent toxicity. The article is highly recommended to anyone interested in the mechanisms of nephrotoxicity.

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