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Apoptosis in HK-2 cells after cisplatin treatment

Jong Ju Kim[1], Eun-Jeong Sim[1], Ki Soo Yoo[1], Young Hyun Yoo[1], Yong Keun Kim[2] and Jong-Min Kim[1]

[1]*Department of Anatomy and Cell Biology, College of Medicine, Dong-A University, Busan, Korea*

[2]*Department of Physiology, School of Medicine, Pusan National University, Busan, Korea*

Cellular and molecular mechanisms responsible for cisplatin-induced nephrotoxicity to renal tubular epithelial cells are not well known. The HK-2 cells (a human renal tubular epithelial cell line) have chosen for the present study, and the potential cell death after cisplatin exposure has been monitored initially by flow cytometry and followed by western blot analyses of apoptosis-related proteins as well as mitogen-activated protein kinases (MAPK). Low concentration (1-10uM) of cisplatin treatment did not significantly increase the apoptosis of HK-2 cells for 48 hours. At least, 25 uM concentration of cisplatin was required to induce a significantly increased level of cell death at 48 hr. Time-course experiment with 25 uM cisplatin showed that the increased rate of G2/M phase at 48 and 72 hrs was remarkable. Overall, cell cycle analysis revealed that HK-2 cells are not readily killed by cisplatin. After cisplatin (25 uM) treatment, phospho-p53 and Bax protein contents were significantly elevated at 48 and 72 hrs. Inhibitors of apoptosis proteins such as survivin and X-chromosome linked inhibitor of apoptosis proteins were also increased. Finally, activation of caspase-3 occurred at 48 and 72 hrs after treatment suggesting that cisplatin-induced HK-2 cell apoptosis is caspase-3 dependent. MAPK activation was not prominent in HK-2 cells after cisplatin treatment which indicates that MAPK system might have a minimal role in HK-2 cell survival and/or apoptosis.

Keyword : Cisplatin, renal epithelial cell, apoptosis