

Abstract Type : Poster

Abstract Submission No. : PO-1315

PARP activation during cisplatin nephrotoxicity in zebrafish and mice

Jinu Kim¹, Myoung-Jin Kim², Jehee Lee²

¹Department of Anatomy, Jeju National University School of Medicine, Korea, Republic of

²Department of Department of Marine Life Sciences & Fish Vaccin Research Center, Jeju National University, Korea, Republic of

Objectives: Cisplatin treatment in cancer therapy has a major side effect in that it causes nephrotoxic acute kidney injury, leading to a high mortality. Here, we developed a novel model to induce cisplatin nephrotoxicity in adult zebrafish of AB wild-type.

Methods: We measured cisplatin-induced proximal tubular dysfunction using fluorescein-labeled dextran uptake and alkaline phosphatase stain in zebrafish. We also measured histological injury of kidney tubules using tubular injury score of periodic acid-Schiff-stained kidney sections in zebrafish.

Results: We demonstrated that intraperitoneal administration of cisplatin caused a decline of kidney proximal tubular function. We also showed that cisplatin-induced a histological injury of kidney tubules. As shown in a C57BL/6 mouse model of cisplatin nephrotoxicity, the activation of poly (ADP-ribose) polymerase (PARP), an enzyme implicated in cisplatin-induced cell death, was markedly increased after injecting cisplatin to zebrafish. Furthermore, pharmacological inhibition of PARP using specific PARP inhibitor PJ34 or 3-aminobenzamide ameliorated kidney proximal tubular function and histological structure in cisplatin-injected adult zebrafish kidneys, showing an additive effect after combination treatment with both inhibitors. This combination effect was also confirmed in the mouse model of cisplatin nephrotoxicity.

Conclusions: These data suggest that adult zebrafish is not only suitable for drug screening, but also useful as a model to study the pathophysiology of cisplatin nephrotoxicity. (NRF-2016R1C1B2012080)