Effect of pan-caspase inhibitor in *ex vivo* cold ischemia-rewarming injury model

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Background: Although the mouse model of vascularized kidney transplantation is a powerful tool for investigating the mechanisms of cold ischemia-reperfusion injury (IRI), the surgery is technically difficult. Here, we evaluated the utility of *ex vivo* cold IRI model with pan-caspase inhibitor (Z-VAD-FMK), which is effective in cold IRI using mice.

Methods: We subjected C57BL/6 mice to intracardiac injection of pan-caspase inhibitor or vehicle. After 24 hours of incubation in 4°C histidine-tryptophan-ketoglutarate solution, the kidney tissue was suspended on a 96-well plate. So, incubation was performed at 37°C for 3, 6, and 9 hours, respectively. Then the kidneys were harvested for histology, western blot, reverse transcription polymerase chain reaction, and immunostaining to assess the effects of pan-caspase inhibitor.

Results: The pan-caspase inhibitor-treated group did not significantly improve histological tubular injury than that of the control group. However, pan-caspase inhibitor ameliorated the magnitude of an increase in kidney injury molecule-1 levels in culture media at 3, 6, and 9 hours after rewarming and was significant at 6 hours. In addition, pan-caspase inhibitor did not show a decrease in proinflammatory cytokines but attenuated apoptosis in renal tubular cells.

Conclusions: Our data demonstrated that pan-caspase inhibitor reduced tubular injury in the *ex vivo* rewarming model after mouse kidney cold preservation.

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