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Acute Kidney Injury

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The effects of the inhibition of p38MAPK on ischemic reperfusion injury

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Background: The incidence of acute kidney injury (AKI) has increased every year, which has major clinical implications, such as increased mortality rate and increased risk of progression to renal failure. P38 mitogen-activated protein kinase (MAPK), a serine/threonine kinase, has been reported to play a crucial role in inflammatory and apoptotic mechanism. We hypothesized that p38MAPK involves in the development and progression of AKI.

Methods: P38MAPK inhibitor (SB-731445) was dissolved in dimethyl sulfoxide (DMSO) and was intraperitoneally-injected at 5 mg/kg (a total volume of 500μl) 3 hours before bilateral vessel clamping in wild type C57BL/6 mice. Control mice received DMSO alone. Kidney tissues from mice were obtained after 48 hours. In addition, human kidney-2 cell line was subjected to be treated with DMSO/SB-731445 and put in the hypoxic incubator (1% O2, 5% CO2, and 94% N2) for 6 hours.

Results: After 48 hours, blood urea nitrogen and serum creatinine concentrations in mice receiving SB-731445 decreased compared to those of mice receiving DMSO alone. The infiltration of inflammatory cells was also alleviated in mice receiving SB-731445 compared with mice receiving DMSO alone. Furthermore, the expression of cleaved caspase-3 significantly decreased in mice receiving SB-731445 compared to in mice receiving DMSO alone. *In vitro,* hypoxic injury during 6 hours resulted in the increased expression of phosphorylated p38MAPK. Treatment of SB-731445 (1-μM) in hypoxic condition attenuated the expressions of inflammatory and apoptosis markers.

Conclusion: p38MAPK is related to the development and progression of AKI. The inhibition of p38MAPK could have protective effects in inflammation and apoptosis related to the development of AKI.

Keywords: acute kidney injury, Ischemia-reperfusion injury, p38MAPK