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The Role of Macrophage Stimulating Protein and its Receptor RON in Renal Ischemia-reperfusion Injury

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Objective: Macrophage stimulating protein (MSP) and its receptor RON, recepteur d'Origine nantais, play an important role in the cell proliferation and migration. In the kidney, tubular and mesangial cells express RON and, hence, MSP/RON pathway may have a role in the renal inflammatory disorders. We have investigated the role of MSP/RON pathway in tubule regeneration in ischemia-reperfusion (IR) injury.

Materials & Methods: We induced bilateral renal IR injury by clamping the both renal pedicles for 30 min in C57BL/6 mice, and sacrificed on 1 or 5 days after IR injury. The expression of MSP, RON, COX-2, Bcl-2 and Bax was determinded in the kidney by immunoblotting. The mRNA level of IL-1β and TNF-α was measured by real-time PCR. Human renal proximal tubular (HK-2) cells were incubated with hydrogen peroxide (H_2O_2) for 24h at different concentrations of MSP, and cell viability was measured by MTT assay. The protein expression of mitogen-activated protein kinases (MAPK), and nuclear factor-kappa B (NF-κB) was detected by immunoblotting.

Results: Plasma creatine was markedly increased on day 1 after induction of IR injury compared with controls, which was attenuated on day 5. Accordingly, Bax/Bcl2 ratio and COX-2 expression in the kidney was increased on day 1, which was markedly attenuated on day 5. The expression of MSP was upregulated, but RON was markedly decreased in both day 1 and day 5 in IR injury rats. H_2O_2 treatment decreased the cell viability in HK-2 cells, which was counteracted by MSP co-treatment. In addition, MSP stimulated tubular epithelial HK-2 cell proliferation in H_2O_2- induced apoptosis through the inhibition of MAPK and NF-κB pathways.

Conclusions: The protein expression of MSP was increased during the regeration of injured tubular cells in I/R injury, and MSP attenuated H2O2-induced cellular damage in HK-2 cells through the modulation of MAPK and NF-κB pathways, suggesting a beneficial potential role of MSP/RON in renal tubule cell regenaration.

Key words: 허혈 재관류 손상, MSP, RON
MSP, RON, renal IR injury