

Kidney Injury Molecule-1 (Kim-1) Expression During Damage and Recovery Phase after Ischemia/Reperfusion Injury in Mouse Kidney

Kyoung-Jin Jung, Jinu Kim, Ki Young Kim, Hee-Seong Jang, Kwon Moo Park

Department of Anatomy and BK21 program, Kyungpook National University School of Medicine

Background : Kidney injury molecule-1 (Kim-1) is a type-1 transmembrane protein. It is not expressed in normal kidney tissue, but expressed at very high levels in human and rodent kidneys with dedifferentiation and proliferation proximal tubular epithelial cells after ischemic or toxic injury. The role of Kim-1 during damage and recovery phases after renal I/R injury remains to be defined. Thus we investigated Kim-1 expression in post-ischemic mouse kidneys.

Method : Experiments were performed in age-matched (8-10 weeks) BALB/c male mice. To induce ischemia, mouse renal pedicle was occluded for 30 min using microaneurism clamp. To determine cell proliferation, bromodeoxyuridine (BrdU, a analogue of thymidine) was administered 20 hrs before harvests of kidneys. Kim-1 expression was evaluated by immunohistochemistry and Western blot analysis using anti-Kim-1 antibody.

Results : Thirty min of bilateral ischemia significantly increased plasma creatinine and blood urea nitrogen (BUN) concentrations from 4 hrs after ischemia. Kim-1 expression was significantly increased from 1 hr after I/R and sustained for up to 16 days. To characterize Kim-1 expression in nephron segments kidney sections were stained using anti-aquaporin-1 (AQP-1, a marker of thin descending limb of Henle's loop), -AQP2 (a marker of collecting duct), -Na⁺-K⁺-Cl⁻ cotransporter (NKCC2, a marker of thick ascending limb, -H⁺-ATPase (a marker of intercalated cells of collecting duct), and Na⁺/K⁺-ATPase antibodies. Kim-1 was detected tubule in the proximal epithelial cells and descending limb of Henle's loop. Kim-1 expression was peaked in 24 hrs. Cell proliferation, as it was determined by BrdU staining, was peaked 3 days after I/R. Kim-1 expression was positively correlated with cell proliferation.

Conclusion : Post-ischemic Kim-1 expression was correlated with cell proliferation. It suggests that Kim-1 play an important role in the restoration of morphological integrity and function to post-ischemic kidney.