F-E7

Role of Akt/PKB Signaling in Kidney Resistance Afforded by Ischemic Preconditioning

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

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

Prior kidney ischemia/reperfusion (I/R) renders the kidney resistant to a subsequent I/R insult. The molecular mechanisms remain to be defined. Serine threonine kinase/protein kinase B (Akt/PKB) signal pathway plays a critical role in the regulation of cell survival and apoptotic death. In this study, we investigated the role of Akt signal pathway on the kidney resistance afforded by previous ischemia/reperfusion in mice. All experiments were performed with BALB/c male mice. To induce ischemic preconditioning, mouse was subjected to 30 minutes of bilateral renal ischemia by clamping renal pedicles with microaneurysm clamps on day 0. An activation of Akt was determined by Western blotting using phospho-Akt antibody. DNA fragmentation as an index of apoptotic cell death was evaluated by DNA ladder and terminal transferase-mediated dUTP nick end-labeling (TUNEL) assay. Plasma creatinine and blood urea nitrogen (BUN) were measured to evaluate renal functions. The level of phosphorylated-Akt was higher in preconditioned mouse kidneys than in non-preconditioned mice. Thirty and ninety min after I/R the level of phosphorylated-Akt was significantly higher in preconditioned mouse kidneys than in non-preconditioned. In consistence Akt the phosphorylation of Bad, which is phosphorylated by active Akt, resulting in an inhibition of apoptotic cell death, was higher in preconditioned mouse kidneys than in non-preconditioned after I/R. After ischemia, DNA fragmentation and the number of TUNEL-positive nuclei were significantly lower in preconditioned mouse kidneys than in non-preconditioned. Post-ischemic increases of plasma creatinine and BUN were much less in preconditioned mice than in non-preconditioned. In conclusion, these results demonstrate that the kidney resistance afforded by previous ischemia/reperfusion is associated with increased anti-apoptotic Akt signal pathway.