PKCα Activation is Protective Against Ischemia-Reperfusion Injury

Chet R. Villa, Yehia Marreez, Gerald W. Dorn II, Harvey S. Hahn
Division of Cardiology, Department of Medicine

Background: PKC isoforms have been demonstrated to have important effects on ischemic preconditioning. The roles of PKCδ and ε have already been described, but the role for PKCα, the most abundant isoform in the heart, has yet to be studied. **Rationale**: Since PKCα, in parallel with PKCδ and ε, translocates with ischemia we hypothesized that it may also play an important role in the heart's response to ischemia-reperfusion injury. **Methods:** Mice expressing peptides that activated (AC) or inhibited (IC) PKCα translocation were compared to littermate controls using an isolated heart global ischemia model. Effluent was collected from the hearts during reperfusion for creatine kinase (CK) analysis and hearts were frozen for molecular signaling studies following ischemia-reperfusion. **Results:** Animals expressing the PKCα activating peptide (AC) demonstrated enhanced functional recovery of LV contractile performance as measured by dP/dt (NTG; 2231.2$\pm$311.9, IC;2332.0$\pm$247.9 v 3619.02$\pm$479.9, $p<0.05$ AC v both). Furthermore, cell survival, measured by CK release, was significantly enhanced in the PKCα activated hearts as compared to PKCα inhibited and non-transgenic controls (NTG;882.33+218.3, IC;794.6+189.4, v AC;158.9+54.5, $p<0.05$ AC v both). There was no effect on basal cardiac function or CK between the three mice lines. **Conclusions:** PKCα activation exerts a protective effect during ischemia-reperfusion injury similar to that of PKCε. This suggests PKCα as a potentially useful therapeutic target in human ischemic heart disease.