SIGNIFICANCE STATEMENT

Ischemic preconditioning is a physiologic adaptation to a transient ischemic event that confers protection against subsequent ischemic injury. Depending on the organ under study and the method of ischemic preconditioning, the adaptive response to ischemia is variable. Although some of the signaling pathways responsible for ischemic preconditioning have been identified, the mechanism of cellular adaptation remains incompletely understood. In this communication, we show that delivering plasmids encoding isocitrate dehydrogenase 2 to kidneys confers resistance to subsequent ischemic injury and increases states 2 and 3 mitochondria respiration. These are similar changes to those observed in mitochondria isolated from ischemic preconditioned kidneys. This work shows that it is possible to use gene delivery to confer resistance to subsequent ischemic injury.