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**IS ZINC CRITICAL FOR MYOCARDIAL REPERFUSION INJURY?**

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**Objectives** The purpose of this study was to investigate the role intracellular free zinc in myocardial reperfusion injury.

**Methods** Isolated perfused rat hearts were subjected to 30 min ischaemia followed by 2 h of reperfusion. Myocardial infarct size was measured with TTC. Cardiac tissue zinc levels were measured with ICPOES. Western blotting analysis was used to probe intracellular signalling events. Cardiac H9c2 cells were subjected to hypoxia/reoxygenation and zinc transporter mRNA expression levels were detected with RT-PCR.

**Results** Cardiac zinc levels were dramatically decreased upon reperfusion in rat hearts and this was prevented by the adenosine A2 receptor agonist NECA. NECA given at reperfusion reduced infarct size, an effect that was blocked by the zinc chelator TPEN. Ischaemic postconditioning consisted of 6 cycles of 10 s ischaemia and 10 s reperfusion also prevented cardiac zinc loss at reperfusion and TPEN abolished the anti-infarct effect of postconditioning. In H9c2 cells, reoxygenation caused cellular zinc loss and enhanced mRNA expression of the zinc importer Zip2. Down-regulation of Zip2 expression with its siRNA exacerbated hypoxia/reoxygenation injury.

**Conclusions** Cellular zinc loss upon reperfusion accounts for the pathogenesis of myocardial reperfusion injury and prevention of zinc loss leads to cardioprotection against reperfusion injury. Increase in Zip2 expression at reperfusion may serve as an important protective mechanism by which cardiac cells are resistant to reperfusion injury.