**DOES CARDIOPLEGIA PROVIDE CARDIAC PROTECTION BY INDUCING Nf-E2 RELATED FACTOR-2 (Nrf2)?**

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**Abstract**

Background. Open heart surgery is often an unavoidable procedure for treatment of cardiovascular disease. Myocardial ischemia-reperfusion injury (MIRI) can occur as a result of cardiopulmonary bypass. The multifaceted mechanisms of MIRI involve the generation of proinflammatory mediators and increases in reactive oxygen species (ROS), resulting in damage to proteins, lipids, and DNA, ultimately impacting postoperative cardiac function and outcomes. Nf-E2 related factor-2 (Nrf2), a basic leucine zipper transcription factor, is regarded as one of the most important regulators in antioxidant pathways. Nrf2 binds to and activates the Antioxidant Response Element (ARE) in the promoters of many antioxidant and detoxification genes.

Purpose. We addressed whether or not cardioplegic solutions induce the activation of Nrf2, therefore serving to protect the myocardium from MIRI.

Methods. We used adult cardiomyocytes in culture to test whether or not four different types of cardioplegic solutions induce Nrf2. The conditions tested include routine laboratory cell culture at 37°C and hypothermic temperatures of 10-20°C.

Results. Our data show that certain cardioplegic solutions caused increases in Nrf2 protein levels under both cell culture and hypothermic conditions. ARE luciferase reporter assay confirmed Nrf2 activation by the cardioplegic solutions. Both High K and Del Nido showed reliable activation of Nrf2.

Conclusions. Our data supports our hypothesis that cardioplegic solutions can be cardiac protective via the activation of Nrf2.

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