The Protective Effects of Insulin in Cardiomyocytes against Iron-mediated Cell Death

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When a cardiac injury occurs as a result of hemolysis, the heart suffers from an intramyocardial hemorrhage and left ventricular remodeling. Studies are showing that the result of this damage is an accumulation of excess ferric iron, and this leads to cell death that correlates with cardiac dysfunction. The mechanistic target of rapamycin (mTOR) is a key downstream signaling pathway that is sufficient for cardiomyocyte (CM) cell survival against iron and responds to a growth hormone called insulin. It is hypothesized that insulin can reverse the harmful effects of excess iron and increase cell survival in CMs. Using H9c2 cardiomyoblasts, originally derived from an embryonic rat ventricle, the effects of insulin in CM cell survival against excess iron were examined. The cells were pre-treated with varying dosages of iron(III) citrate before applying insulin. Cell viability was assessed using a Live/Dead Assay, in which live cells were stained with calcein AM (green) and the nuclei of dead cells were stained with ethidium homodimer-1 (red). In comparison to the amount of cell death caused by iron alone, insulin increased cell proliferation substantially ($p<0.05$). In addition to this, a western blot analyzed the protein expression in relation to the mTOR signaling pathway. The results suggest that insulin has the potential to mediate iron-induced CM death. Overall, this could lead to an improved approach to treating various cardiovascular diseases and preventing heart failure.

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