EP1_5

Resveratrol and Sirtuin 6 Protects the Cardiomyocytes Against Ischemic Damage

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Ischemic injury is the leading cause of death in Western countries. Enormous interest has therefore arisen concerning the mechanisms capable of limiting myocardial damage. The proposed study is aimed at development of approaches to reduce ischemic damage through the use of sirtuin pathway and to elucidate the mechanism of the cardioprotection. Resveratrol (RSV), a polyphenol abundantly found in grape skin and red wine, has been shown to promote protection against ischemic injury in the heart in an unknown mechanism. RSV is also known to increase sirtuins, which are enzymes that modulate diverse biological processes. The objective of this study is to explore whether sirtuins are mediators in ischemic protection and whether RSV provides protection through the pathway of sirtuins. For that purpose we subjected cardiomyocytes from transgenic mouse (TG), with over expression of sirtuin6, to ischemic stress. The hypothesis of this study was that cardiomyocytes from transgenic mouse subjected to prolonged ischemia, may over release survival factors compared with WT mice, that will protect the naïve cardiac cells from the ischemic stress. In parallel experiments, neonatal rat cardiomyocyte cultures were treated with RSV 24 h before subjected to hypoxia. In both experiments we received protection from ischemic damage. The results were proved by LDH and CK released and Propidium Iodide binding after the ischemia. We found, by Western blot analysis, that the protective mechanism of RSV treatment includes activation of p-AMPKα pathway, decrease reactive oxygen species (ROS), increase sirtuin1 and sirtuin6 protein levels. The protective mechanism by over-expression of sirtuin6 includes activation of p-AMPKα pathway, increase protein level of Bcl2, inhibition of NFkB, decrease of ROS and a decrease in protein level of p-AKT. All these processes prevent necrosis/apoptosis, protect cardiac cells from ischemic stress, and lead to myocardial survival.