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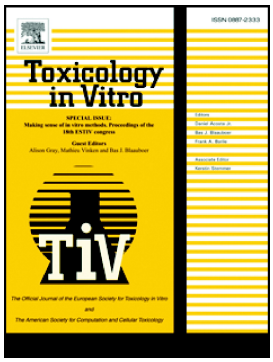

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Michela Pecoraro, Aldo Pinto, Ada Popolo

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Inhibition of Connexin 43 translocation on mitochondria accelerates $CoCl_2$-induced apoptotic response in a chemical model of hypoxia

Michela Pecoraro, Aldo Pinto and Ada Popolo*

Department of Pharmacy, University of Salerno. Via Giovanni Paolo II, Fisciano, Salerno
* corresponding author
apopolo@unisa.it

Abstract

Hypoxia is the basis of many myocardical conditions, and it can initiate cell death programs, among which apoptosis is the well-known. Connexin 43 (Cx43), the major component of cardiomyocyte Gap Junctions, is important in cardioprotection. Cx43is involved in ischemia/reperfusion injury and ischemic preconditioning's protection in vitro; however, its role on cardiomyocyte under hypoxia is still unclear. Reports have shown that Cx43 is also located at the inner membrane of mitochondria where it has been implicated in enhanced ischemic preconditioning response.

In this study, to evaluate the role of mitochondrial Cx43 in hypoxia, we used an in vitro model of chemical hypoxia induced by Cobalt chloride ($CoCl_2$) in H9c2 cell line. $CoCl_2$ (50-100-150µM) was administered for 3 or 6h, alone or combined with Radicicol, that inhibits Cx43 translocation on mitochondria, to demonstrate the crucial role of mitochondrial Cx43 in the cardioprotection. In fact, reduction of Cx43 translocation on mitochondria increases mitochondrial ROS production, cytosolic and mitochondrial calcium overload and mitochondrial membrane depolarization, thus resulting in an increase of the triggering apoptotic pathway.

In conclusion, our study demonstrates the involvement of mitochondrial Cx43 in the apoptotic process in a chemical hypoxia model and suggests that mitochondrial Cx43 plays a crucial role in cytoprotection.

Keywords: Connexin 43, chemical hypoxia, apoptosis, Cobaltum chloride

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