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CONNEXIN 43 PLAYS AN IMPORTANT ROLE IN THE MOLECULAR MECHANISMS IMPLICATED IN ISCHEMIC PRECONDITIONING

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The heart is one of the most energy demanding tissues in the body and is totally dependent upon oxidative phosphorylation to supply the large amount of ATP that requires. The heart can usually survive a short period of ischaemia and then recover upon reperfusion, but this mechanism can exacerbate the damage that takes place during the ischemic period. There is increasing evidence that mitochondrial dysfunction plays a central role in mediating the main components of reperfusion injury, and that one of the most effective ways of protecting hearts from such injury is the ischemic preconditioning (IP). It has been clearly demonstrated that connexin 43 (Cx43) is located in the cardiomyocyte mitochondria and is important for the cardioprotection by IP (Boengler et al., 2005; Heinzel et al., 2005; Rodríguez-Sinovas et al., 2006). Moreover, IP does not occur in transgenic mice Cx43KI32, which have Cx32 instead of Cx43 (García-Dorado et al., 2007), being consistent with the possible role of Cx43 in IP. There are also several pharmacological agents, such as diazoxide, that delay the death of ischemic myocytes when the myocardium is pretreated with the agent before an episode of ischaemia (Grover et al., 2000; Scwartz et al., 2002; Gross et al., 2003). However, the mechanisms underlying these processes remains unclear.

To elucidate the molecular mechanisms implicated in IP and the role of Cx43, we are performing a comparative differential expression proteomics study of mitochondrial proteins from cardiomyocytes in preconditioned rats, in transgenic Cx43KI32 mice and in rats pretreated with two different pharmacological agents known to induce preconditioning. The samples were analyzed by stable 18O isotope-labeling, IEF separation and linear ion trap mass spectrometry and quantified using the program QuiXoT. The results obtained to date suggest that Cx43 affects the functions that are altered in IP.