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Dipyridamole increases Cx43 expression in heart muscle cells through Adenosine 2A receptor/PKC pathway

Francesco Bianchi, Stefania Moscato, Chiara Ippolito, Sauro Dini, Antonietta R.M. Sabbatini, Amelio Dolfi, Letizia Mattii

Dept of Clinic and Experimental Medicine, Sect. Histology, University of Pisa, Pisa, Italy

Cx43, a predominant connexin in the heart, forms gap junctions (GJs) that facilitate electrical cell-cell coupling and hemichannels that represent a pathway for the exchange of ions and metabolites between cytoplasm and the extracellular milieu. Our recent results (1) demonstrated that an altered distribution and quantitative expression of factors involved in Cx43-made GJ regulation as Cx43, its phosphorylated form pS368-Cx43, PKC phosphorylated substrates, and adenosine 2A receptor ($A_{2A}R$) are present in ventricular myocardium with left ventricular dysfunction. Moreover, dipyridamole treatment, which shows a mild protective role on left ventricular function, seems to act through re-modulating the expression and activation of these factors. The role of these factors on signal transduction cascade triggered by dipyridamole was evaluated in this study by pharmacological and immunoistochemical experiments using the rat cardiomyoblast cell line H9c2. The treatment of H9c2 cells with dipyridamole enhanced the expression of Cx43, $A_{2A}R$ and PKC activity while induced a decrease of pS368-Cx43. Interestingly, we found that the $A_{2A}R$ activation was a prerequisite for the effects of dipyridamole, in fact, the pre-treatment with CSC, a selective $A_{2A}R$ receptor antagonist, abolished its effects on the expression of these factors.

References

[1] Bianchi et al. (2014). Effect of dipyridamole on gap junctions regulation in diseased myocardium. IJAE 119(1)supplement, 18.

Keywords

Heart cells; Cx43; PKC; adenosine receptor; dipyridamole.