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Characterization of three PDE5 isoforms in murine cardiomyocytes

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Phosphodiesterase 5 (PDE5A) is responsible for hydrolysis of cGMP, a second messenger regulating many physiological functions in cardiac myocytes. PDE5A involvement in cardiac hypertrophy has been reported and the use of its inhibitor, sildenafil, has reverted the pathological increase of cardiac size in humans and in animal models (Nagendran et al., 2007). In humans, a single PDE5 gene encodes for three isoforms (PDE5A1, A2 and A3), which differ in their N-terminus being translated from alternative initiation sites (Lin et al., 2000). The isoforms exhibit specific tissue expression patterns and different sensitivities to pharmacological inhibitors. However, little is known about their specific biological roles.

The existence of three murine PDE5A isoforms was predicted through human gene homology and confirmed by RT-PCR. Tissue expression pattern of each variant was uncovered by RT-PCR and western blot analysis. In adult heart, transcripts encoding for the three isoforms were detected. In cardiomyocytes primary cultures and cell lines PDE5A isoforms localization was revealed by fluorescence microscopy analysis and subcellular fractioning. Their phosphodiesterasic activities and sildenafil sensibilities were measured by radioactive assays. Finally, post-translational modifications were explored. Hypertrophic stimuli resulted in Ser 92 phosphorylation of PDE5A isoforms, possibly through by Protein Kinase A.

In summary, the understanding of PDE5A isoforms localization and differential activation and activity might be an important step toward the improvement of the diagnostic, prognostic, and predictive values of PDE5A in hypertrophy treatment.

References

[1] Nagendran et al. (2007). Phosphodiesterase type 5 is highly expressed in the hypertrophied human right ventricle, and acute inhibition of phosphodiesterase type 5 improves contractility. Circulation. 116:238-48.
[2] Lin et al. (2000) Identification of three alternative first exons and an intronic promoter of human PDE5A gene. Biochem Biophys Res Commun 268: 596–602.

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