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PDE5 inhibition counteracts β- adrenergic induction of cardiac hypertrophy

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The β-adrenoreceptors play important roles in cardiovascular function regulation mediated by the sympathetic nervous system. It is known that sustained β-adrenergic stimulations promotes cardiac hypertrophy (Oleg et al., 2007). Recently an antihypertrophic role of sildenafil, that acts as a phosphodiesterase 5 (PDE5) inhibitor, has been demonstrated in mice where hypertrophy was mechanically induced (Takimoto et al., 2005). We report the results obtained on a cellular system of cardiac hypertrophy in vitro. By using three-dimensional cultures of mouse ventricular cardiomyocytes (Xiang et al., 2005) and isolated cardiomyocytes we show that: 1) these cells express levels of PDE5 comparable with the ones in normal heart, 2) treatment of the cultures with the β-adrenoreceptors agonist isoproterenol induces cell hypertrophy accompanied by an increment of the level of PDE5 expression and 3) sildenafil prevents the development of such hypertrophy through specific β-adrenoreceptors and signaling pathways 4) the inhibition of other members of PDE family might contribute to the prevention of hypertrophy following β-adrenergic stimulation. In summary, we present a test system that may contribute to clarify intracellular signaling pathways leading to cardiac hypertrophy and to identify molecular targets, like the ones involved in PDE5 activity, on which to steer the development of new drugs and to design new clinical therapies.

References

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