BMC Pharmacology



Poster presentation

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cGMP-Protein kinase G signaling pathway is involved in stimulation of Leydig cell steroidogenesis

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from 3^{rd} International Conference on cGMP Generators, Effectors and Therapeutic Implications Dresden, Germany. 15–17 June 2007

Published: 25 July 2007

BMC Pharmacology 2007, 7(Suppl 1):P34 doi:10.1186/1471-2210-7-S1-P34

This abstract is available from: http://www.biomedcentral.com/1471-2210/7/S1/P34

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The androgen-secreting Leydig cells produce cGMP, but the pathways responsible for generation, degradation, and actions of this intracellular messenger have been incompletely characterized in these cells. Here, we show the presence of mRNA transcripts for several elements of cGMP signaling pathways in purified rat Leydig cells from adult animals, including the membrane-bound and soluble guanylyl cyclases, endothelial and inducible nitric oxide synthases, the cGMP-specific phosphodiesterase 5, the protein kinase G (PKG), the multidrug resistance protein 5, and the rode, cone, and olfactory cyclic nucleotidegated channels. Increase in cGMP levels induced by stimulation of membrane-bound and soluble guanylyl cyclase activities and inhibition of phosphodiesterase 5 activity as well as the addition of a cell permeable cGMP analog increased basal and agonist-stimulated androgen production in vitro. Moreover, inhibition of soluble guanylyl cyclase and PKG activities was accompanied with attenuated androgen production. Immunoprecipitation study showed phosphorylation of the steroidogenic acute regulatory protein upon the treatment with nitric oxide donors, which was abolished by the addition of a PKG inhibitor. These results suggest that cGMP contributes to the control of androgen production in Leydig cells through PKG-dependent phosphorylation of steroidogenic acute regulatory protein.