CAMP-SPECIFIC PHOSPHODIESTERASE 8A IS LOCALIZED IN MITOCHONDRIA OF GRANULOSA CELLS AND REGULATES PROGESTERONE SYNTHESIS

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Abstract Body

cAMP-specific phosphodiesterase 8A is localized in mitochondria of granulosa cells and regulates progesterone synthesisAmel Lounas, Christine Guillemette, François Richard*Centre de recherche en reproduction, développement et santé intergénérationnelle (CRDSI), Département des sciences animales,Faculté des Sciences de l'agriculture et de l'alimentation, Université Laval, Québec, Québec, Canada, G1V 0A6

In mammalian cells, steroidogenesis is widely regulated by the intracellular concentration of the cyclic nucleotide cAMP which are regulated by 3',5'cyclic nucleotide phosphodiesterases (PDEs). The expression of PDEs in ovarian follicular cells may contribute to the specificity and the width of cAMP responses. Recent works have characterised PDE8 family in Leydig cells as a regulator of steroidogenesis. In the present study, we showed that in swine PDE8A transcript and protein were expressed in granulosa cells, cumulus cells and oocyte. The functional presence of PDE8 measured as IBMX-insensitive cAMP-PDE activity was detected in both granulosa cells and isolated mitochondria supporting the functional presence of PDE8A in mitochondria. PDE8a protein was detected by western blot in isolated mitochondria and co-localisation of immune-reactive PDE8A signal and mitotracker labelling further supports functional localisation of PDE8A in mitochondria. Because mitochondria are a key organelles in steroidogenesis, the effect of PDE8a on progesterone production was assessed using dipyridamole as specific PDE8 inhibitor in cumulus-oocyte complexes. A significant effect was measured in presence of dipyridamole suggesting the functional contribution of PDE8A in steroidogenesis. These results demonstrate that the PDE8A is functionally present in granulosa cells and cumulus-oocyte complexes. Since mitochondria is one of the localisation of PDE8A, the effect of the specific PDE8 inhibitor on progesterone secretion supports the mitochondrial contribution of PDE8A in steroidogenesis.