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Differential Effects of Specific Phosphodiesterase Isoenzyme Inhibitors on Bovine Oocyte Meiotic Maturation

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Abstract

The differential regulation of cAMP levels within the oocyte and somatic (cumulus) cell compartments of the bovine follicle, and the subsequent regulation of oocyte meiotic maturation was examined through specific cell-type localisation of phosphodiesterases (PDEs). Selective PDE inhibitors were used to modulate cAMP levels in each of the two follicular compartments and to examine their effects on oocyte meiotic maturation. Ovaries were obtained from an abattoir and cumulus-oocyte complexes (COC) were aspirated from antral follicles into culture medium supplemented with 4 mg/ml BSA and 2mM 3-isobutyl-1-methylxanthine (IBMX). COC, denuded oocytes (DO), or mural granulosa cells (MGC) were cultured either with or without forskolin or FSH, in the presence of specific PDE inhibitors; either milrinone (PDE3 inhibitor), cilostamide (PDE3 inhibitor), or rolipram (PDE4 inhibitor). COC/DO cultures were assessed for meiotic progression and cAMP content, and MGC for cAMP production. The type 3 PDE inhibitor, but not the type 4, prevented spontaneous meiotic maturation and elevated intraoocyte cAMP in cultured denuded oocytes. In contrast, the type 4 PDE inhibitor had no effect on the oocyte, but elevated mural granulosa and cumulus cell cAMP production. The results of this study indicate that specific PDE subtypes are differentially localised within the two compartments of the bovine follicle—the type 3 PDE in the oocyte and the type 4 PDE in the granulosa cells. In addition, oocyte cAMP levels are primarily regulated in bovine oocytes by its degradation by PDE, whereas granulosa cell cAMP levels are controlled mainly by active adenylate cyclase, with both sources able to participate in oocyte meiotic regulation.

Keywords




oocyte; meiotic maturation; meiotic inhibition; cAMP; phosphodiesterase; granulosa cell





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