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Dissociation between the inhibitory and the stimulatory action of cAMP on maturation of rat oocytes

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Summary

The possible mediatory role of cAMP in the induction of oocyte maturation by luteinizing hormone (LH) is not yet clear since evidence for both inhibitory and stimulatory actions of the nucleotide on the oocyte has been provided. To elucidate the role of cAMP in regulation of oocyte meiosis we tried in the present study to dissociate between the inhibitory and stimulatory action of this nucleotide on oocyte maturation. To induce maturation, oocytes enclosed by their follicles were transiently exposed to either dibutyryl cAMP (dbcAMP) or to the phosphodiesterase inhibitor methylisobutylxanthine (MIX). Inhibition of maturation was obtained by the addition of the above agents to either follicle-enclosed oocytes incubated in the presence of LH or isolated cumulus-free oocytes that mature spontaneously *in vitro*. We found that inhibition of oocyte maturation is obtained by a relatively low dose of either dbcAMP or MIX while higher concentrations of these agents are required to induce oocyte maturation. Coupling of the oocyte to the cumulus cells, as expressed by the fraction of labeled uridine transferred from the cumulus cells to the oocyte following exposure of the follicle-enclosed cumulus–oocyte complex to MIX, was also determined. We found that uncoupling of the oocyte from the cumulus cells corresponded with the induction, but not inhibition of oocyte maturation, both by its concentration dependence and time-course. We suggest that cAMP has a dual role in regulation of oocyte maturation. Lower levels of the nucleotide act to maintain meiotic arrest, while elevated levels of cAMP mediate LH action to induce meiosis resumption.

Introduction

Both oocyte maturation and luteinization are included among the responses of the rat ovary to LH (Baker, 1972). While it is clearly evident that luteinization is a cAMP-mediated response (Chan-

ning and Seymour, 1970), the role of cAMP in the induction of meiosis resumption has not been fully elucidated. Moreover, the available data related to the possible involvement of cAMP in regulation of oocyte maturation are contradictory, since they provide evidence for both inhibitory and stimulatory actions of the nucleotide. Tsafirri et al. (1972) have demonstrated that injection of a cAMP derivative into isolated rat follicles could mimic the effect of LH and induce oocyte maturation. In a later study, however, the presence of the

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