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Mouse Oocyte Mitogenic Activity Is Developmentally Coordinated throughout Folliculogenesis and Meiotic Maturation

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Abstract




Oocytes secrete soluble factors that regulate the growth and differentiation of follicular cells, including maintenance of the distinctive cumulus cell phenotype. This study determines whether the mitogenic activity of oocytes is developmentally regulated and examines the responsiveness of follicular cells to oocytes at different stages of follicular development. Prepubertal SV129 mice of varying ages were primed with 5 IU equine chorionic gonadotropin (eCG) and oocytes/zygotes collected either 46 h post-eCG (immature oocytes), 12 h after administration of 5 IU human CG (hCG; ovulated ova), or 12 h post-hCG and mating (zygotes). Mural granulosa cells (MGC) from antral follicles and GC from preantral follicles were cultured \pm denuded oocytes (DO) for 18 h, followed by a 6-h pulse of [³H]thymidine as an indicator of cellular DNA synthesis. Coculturing MGC with meiotically maturing oocytes led to a dose-dependent increase in [³H]thymidine incorporation (20-fold above control levels at 0.5 DO/ μ l). However, [³H] counts remained unchanged from control levels when cultured with meiotically incompetent DO from 11- to 15-day-old mice (3% germinal vesicle breakdown; GVB), irrespective of dose of DO or developmental status of GC (MGC or preantral GC). In some treatments, spontaneous meiotic resumption of competent oocytes was prevented by culturing with 5 μ M milrinone, a selective inhibitor of oocyte-specific cyclic nucleotide phosphodiesterase. The mitogenic capacity of oocytes was found to decline during and after oocyte maturation. [³H]Thymidine incorporation in MGC was highest (11-fold above controls) when cultured with meiotically inhibited (milrinone-treated) GV DO, stimulated 5.5-fold by culture with maturing oocytes, 3-fold with ovulated ova, and unstimulated by zygotes. [³H]Thymidine incorporation in MGC was not altered by the dose of milrinone, either in the presence or absence of DO. Metaphase I marked the beginning of the decline in the capacity of oocytes to promote MGC DNA synthesis. These results demonstrate that the capacity of oocytes to promote proliferation of granulosa cells follows a developmental program, closely linked to oocyte meiotic status, increasing with the acquisition of meiotic competence and declining during and after oocyte maturation.

Keywords






oocyte mitogen; oocyte meiotic competence; folliculogenesis; granulosa cell; oocyte maturation

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