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Mechanisms Involved in the Control of the Meiotic Cell Cycle

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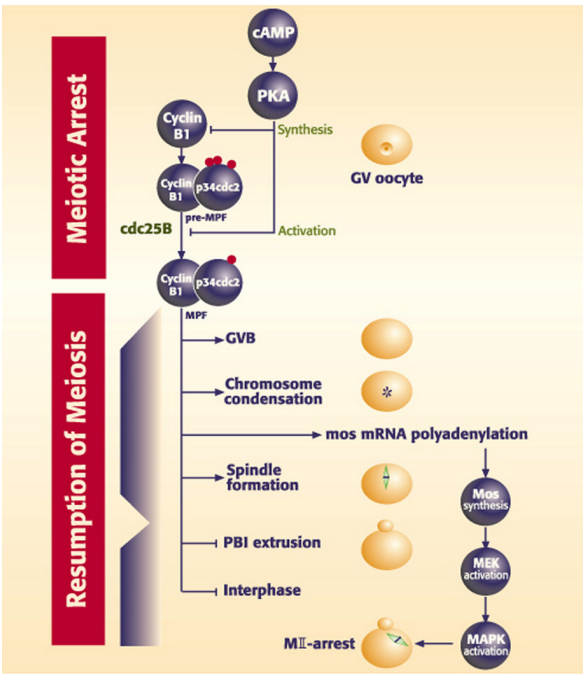
Studies in our laboratory are directed at identification and characterization of molecular events that regulate reproduction and early development. Of major interest is the control of the meiotic status of the mammalian oocyte. Attempts to disclose this issue include investigation of the gating mechanism of the gap junctions that mediate the communication of the inhibitory cAMP from the somatic cells of the ovarian follicle to the oocyte and the response of the ovarian gap junction protein connexin 43 (Cx43) to gonadotropins. Search for complementary mechanisms that ensure the efficiency of a timely alteration between meiotic arrest and resumption of meiosis include cloning and characterization of an oocyte-specific PKA anchoring protein (AKAP) responsible for sequestration of this enzyme and its possible calocalization with the oocyte phosphodiesterase, PDE3A. Potential downstream regulators that are subjected to the PKA-mediated cAMP action are examined and their hierarchy is explored. Specific interest is directed at the role of the anaphase-promoting complex (APC) in degradation of such proteins, in particular, those that participate in regulation of chromosome segregation. A list of ovarian and endometrial genes, the expression of which is upregulated in association with ovulation and implantation, have been recently generated by suppression subtructive hybridization (SSH) and microarray chip analysis respectively. Further attempts to characterize and identify the specific function of a selected group of these genes are presently performed. Our studies on implantation and early embryonal development are also directed at exploration of signals that control the extensive angiogenic response of the uterus to the implanting embryo and its possible association with Cx43 expression.



Regulation of meiosis in mammalian oocytes:
The GV arrested oocyte is maintained at prophase due to the inhibitory effect of a PKA-mediated cAMP action. The inhibition is conferred on two levels: the prevention of pre-MPF activation due to sustained phosphorylation on p34cdc2 and repression of de-novo synthesis of cyclin B1. In response to the preovulatory LH (or following the release of the oocyte from the ovarian follicle) intraoocyte cAMP concentration drops and MPF activation is catalyzed by cdc25B. The active MPF elicits resumption of meiosis, namely GVB, chromosome condensation and spindle formation. MPF activity also stimulates the polyadenylation of mos mRNA, leading to Mos expression and activation of MAPK. Inactivation of MPF at MI is neccessery for the extrusion of PBI, whereas its reactivation at the onset of the second meiotic division suppresses entry into interphase. The MII arrest of the oocyte is endured until fertilization by the action of MAPK.

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