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Biology of Reproduction Highlights . . .

Antagonists of Myosin Light Chain Kinase and of Myosin II Inhibit Specific Events of Egg Activation in Fertilized Mouse Eggs. Sara Matson, Styliani Markoulaki, and Tom Ducibella. Biol Reprod 2006; 74:168-175. Published online ahead of print 5 October 2005; 10.1095/biolreprod.105.046409

Mechanism of mammalian egg activation. Egg activation is a key step in beginning embryogenesis. It is driven by oscillations in free calcium of precise amplitude and frequency. The response to calcium is mediated by calmodulin-dependent protein kinase II (CAMK2), but other downstream targets of calcium and calmodulin (CAM) were unknown. In a paper from the Ducibella lab on p. 168, Matson and Markoulaki show that antagonists of a myosin light chain kinase, MYLK2, did not affect calcium oscillations in fertilized mouse eggs, but did block second polar body production almost completely and reduced cortical granule exocytosis by about 50%. Similarly, an inhibitor of myosin II, a MYLK2-dependent cytoskeletal component of mouse eggs, blocked these specific endpoints of egg activation. These antagonists did not block the onset of anaphase II, but prevented spindle rotation. Therefore, MYLK2 is probably one of a family of CAM-dependent proteins which transduce the calcium signal at fertilization and regulate specific events of egg activation

A Non-Genomic Action of Estradiol as the Mechanism Underlying the Acute Suppression of Secretion of Luteinizing Hormone in Ovariectomized Ewes. J. Alejandro Arreguin-Arevalo and Terry M. Nett. Biol Reprod 2006; 74:201-207. Published online ahead of print 19 October 2005; 10.1095/biolreprod.105.044685

Feedback response switching. One of the long-persistent mysteries in the reproductive neuroendocrine field is the biphasic nature of estradiol feedback. During the female reproductive cycle, in animal models mimicking the cycle, or upon replacement of estradiol to ovariectomized animals, estradiol initially suppresses GnRH and LH release through negative feedback. Once estradiol elevation has been sustained for several hours, the response switches from negative to positive feedback, and robust sustained surges of GnRH and LH are induced. On p. 201 of this issue, Arreguin-Arevalo and Nett provide new insight into this phenomenon. Treatment of ovariectomized ewes with estradiol induced the expected biphasic response. However, when estradiol was conjugated to a larger molecule, preventing its diffusion through the lipid bilayer, only the initial negative feedback phase was observed. This suggests that negative feedback can be mediated by estradiol action at the membrane to activate or repress signaling cascades, whereas positive feedback requires estradiol action via nuclear estradiol receptors, implying changes in gene transcription are involved. This finding will help sculpt future studies into both pituitary and neurobiological mechanisms engaged by estradiol to bring about feedback regulation.

Aging of Male Germ Line Stem Cells in Mice. Xiangfan Zhang, Kevin T. Ebata, Bernard Robaire, and Makoto C. Nagano. Biol Reprod 2006; 74:118-123. Published online ahead of print 21 September 2005; 10.1095/biolreprod.105.045591

Aging in the testis. Although not as dramatically as in the female, male gametogenic potential declines with age. On p. 118 of this issue, in a paper from the Nagano laboratory, Zhang et al. use spermatogonial stem cell transplantation to address the respective roles of germ cells and testicular environment in the age-related decline in function. Transplantation of stem cells from 2-year old atrophied testes into testes of young mice revealed diminished numbers and colonization potential of the aging spermatogonial stem cells. Likewise, transplantation of stem cells from young male donors into testes of 2-year old recipients led to reduced colonization by comparison to transplantation into 1-year old recipients. Thus, these experiments represent a clever approach of the stem cell transplantation assay to a biological problem and provide evidence that both germ cells and the somatic environment contribute to aging effects in the testis.

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