COORDINATING THE TRANSITION FROM EGG TO EMBRYO IN MAMMALS

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At fertilization of mammalian oocytes, the sperm induces a series of increases in the concentration of intracellular Ca^{2+}. These Ca^{2+} oscillations trigger all the events of egg activation, including cortical granule exocytosis, completion of meiosis and entry into the first mitotic division. Thus, intracellular Ca^{2+} plays a pivotal role in coordinating the transition from egg to embryo. Our work is focussed on understanding how the oocyte prepares for fertilisation, how the Ca^{2+} oscillations are controlled and how Ca^{2+} stimulates signalling pathways that lead to optimal early embryonic development. In this lecture I will focus on the downstream pathways of Ca^{2+} signalling at fertilisation. Conventional Protein Kinase C (cPKC) is the major downstream target of Ca^{2+} in many cell functions. Using PKC-GFP fusion proteins we have found that cPKC is recruited to the membrane in a manner that is dependent on the frequency and amplitude of the Ca^{2+} oscillations. Recruitment of cPKC appears to promote the Ca^{2+} influx necessary to sustain the generation of long lasting Ca^{2+} oscillations. In other cell types cytosolic Ca^{2+} increases are known to stimulate mitochondrial respiration. We have found that maintenance of resting Ca^{2+} levels and sperm-induced Ca^{2+} oscillations are critically dependent on mitochondrial ATP production: a feature not shared by many cell types. Since Ca^{2+} release increases ATP consumption we investigated whether the Ca^{2+} transients increase mitochondrial activity so as to meet this increase in demand. Monitoring autofluorescence from NADH and flavoproteins reveals that Ca^{2+} transients stimulate a change in redox state of mitochondria, presumably by activating Ca^{2+}-sensitive dehydrogenases of the TCA cycle. Thus, through activation of downstream pathways, including PKC, cyclin B degradation and mitochondrial activity, intracellular Ca^{2+} provides a signal that orchestrates the activation of early mammalian development.

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