Mechanisms of egg activation and how calcium signalling affects embryonic development

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The mammalian egg arrests at metaphase of the second meiotic division (MetII). Sperm break this arrest and the egg undergoes a series of events collectively termed 'egg activation'. Three important features of egg activation are: a re-initiation of the cell cycle; a block to polyspermy; and a switch-on of genes in early zygotic genome activation. Recently our work has elucidated some of the signalling pathways employed by the sperm in the process of egg activation. All the events of egg activation are induced by the release into the egg of a sperm-borne phospholipase Cζ. This induces a series of calcium spikes. We have identified calmodulin-dependent protein kinase II (CamKII) as the physiological transducer of the calcium spikes, but only in the process of cell cycle resumption and the switch on of early genes. Interestingly CamKII does not induce the release of cortical granules essential for the block to polyspermy. We have identified Emi2 (Early Mitotic Inhibitor 2) as an immediate target of CamKII activity for reinitiation of the cell cycle. Emi2 inhibits the activity of the Anaphase-Promoting Complex (APC), and CamKII-dependent Emi2 phosphorylation induces immediate Emi2 degradation. An increase in APC activity allows completion of the second meiotic division by loss of CDK1 activity and a switch on in separase activity. Loss of Emi2 during oocyte maturation, prevents oocytes from arresting at metII. It is important for the egg to disengage itself from the MetII-arresting proteins at fertilization. Therefore it is unsurprising that a number of studies have demonstrating that alterations in the strength of calcium spiking at fertilization affect embryo development. Some models for this based on our current understanding of cell cycle control during MetII arrest have been developed.