The role of the APC/C inhibitor Emi2 in the regulation of the M-phase checkpoint.

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ABSTRACT

Mammalian oocytes enter meiosis before birth, where they remain arrested at G2/Prophase (>40 years in humans) until they receive the stimulus to enter the first meiotic M-phase (MI).M-phase surveillance in Mitosis and Meiosis I (MI) is regulated by the Spindle Assembly Checkpoint (SAC).SAC, physiologically, inhibits the APC/C so that anaphase onset is delayed until all chromosomes are under tension on the M-phase spindle. After the first meiotic division, subsequently the oocyte enters the second meiotic M-phase and arrests at Metaphase II (MII) awaiting fertilization. MII arrest is maintained through the action of the APC/C inhibitor, Early Mitotic Inhibitor 2 (Emi2). We have found that Emi2 also participates in spindle or chromatin damage-induced MI arrest. Firstly, we have established that Emi2 is enabling an MII-related arrest state in MI. Also we found that Emi2 depleted oocytes, under conditions of spindle/chromosome damage (with Taxol or Nocodazole), fail to launch a MI arrest response to chromosomal instability. This implies that that Emi2, alongside the SAC, functions as a general surveillance factor that may arrest oocytes in M-phase when the spindle or chromosomes are damaged in an M-phase checkpoint. Furthermore, in somatic cells, through FACS analysis and immunostaining protocols we found that Emi2 acts as a cytostatic factor and its expression leads to cell cycle delay or arrest at G2/M.

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