ABSTRACT

The checkpoint kinase 1 (CHK1) is an established effector molecule of ATR-/ATM-dependent signaling pathway, activated in response to DNA damage. However, CHK1 now appears to play also important roles during unperturbed cell cycle. In interphase, CHK1 localizes to centrosomes and negatively regulates entry into mitosis by preventing premature activation of CDK1/cyclin B complex. During S phase, CHK1 is responsible for maintaining the physiological turnover of CDC25A and also functions to coordinate mitotic events through regulation of CDC25B. Moreover CHK1 is required for the spindle checkpoint which protects against spontaneous chromosome mis-segregation. Chk -/- mice are embryonic lethal and therefore a role for CHK1 in meiosis is unknown. This work for the first time reports that CHK1 is involved in meiotic maturation of mouse oocytes. The amount of CHK1 protein increases from GV to MII phase but it`s phosphorylation on Ser317 occures mainly between phases MI and MII. Inhibition of CHK1 kinase activity by SB218078 inhibitor results in delay of GVBD and compromises CDK1 activity. The spindle migration and cortical membrane differentiation is disrupted due to CHK1 inhibition and cytokinesis emerges defectively. In addition spindle assembly checkpoint induced by taxol was partially overcome in SB218078-treated oocytes. CHK1 depletion by RNA interference leads to disturbances in chromosome congression, alignment and segregation. Finally, over-expression of GFP-CHK1 blocks meiotic maturation in GV-stage, CHK1 is localized to the nucleus. These findings indicates that CHK1 has a crutial function in mammalian oocytes and will be the subject of future investigations.