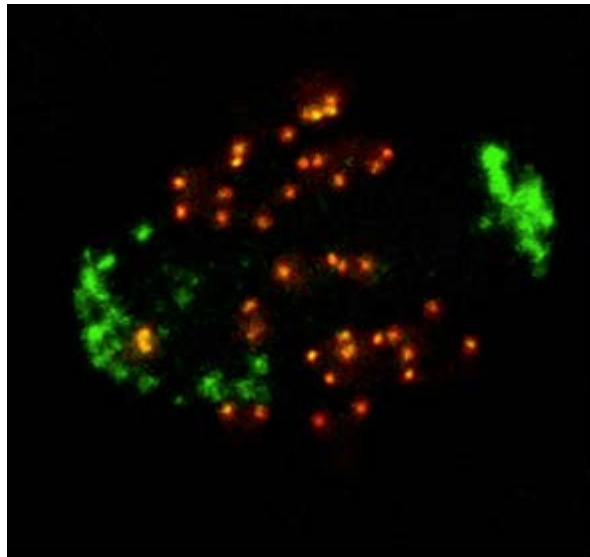


Oocyte maturation directed by PLK1

March 16, 2015— Chromosome segregation is one of the most important events during cell division, both in somatic cells (mitosis) and in germ cells (meiosis). Improper segregation of chromosomes leads to a range of defects in the daughter cells, and nowhere is correct chromosome segregation more crucial than in the division of germ cells as they pass on genetic information to the next generation of offspring. But surprisingly, errors in chromosome segregation are known to occur with high frequencies in mammalian oocytes. Meiosis in oocytes is also unique, as the cell division cycle is arrested for an extended period in prophase I before resuming meiotic division. One factor that plays a major role in cell division is Polo-like kinase 1 (PLK1), a serine/threonine kinase, which has been implicated in multiple events during mitosis. The functions of PLK1 in oocytes undergoing maturation (meiosis), however, are not well understood.

Now, a new joint study by team leader Tomoya Kitajima and colleagues in the Laboratory for Chromosome Segregation and collaborators at the Institute of Animal Physiology and Genetics (Czech Republic) and European Molecular Biology Laboratory (EMBL; Germany) looks at the role of PLK1 during meiosis, using mouse oocytes as a model. Their findings, published in *PLoS ONE*, demonstrate that PLK1 controls meiotic cell division in a manner similar to mitosis, such as promoting microtubule elongation and stabilizing microtubule-kinetochore binding. They also find that PLK1 has functions specific to meiosis such as activating the anaphase promoting complex/cyclosome (APC/C) for entry into anaphase I, for proper chromosome segregation and maintaining chromosome condensation during meiosis I—meiosis II transition.



Movie: Oocyte undergoing first meiotic division. PLK1 (green) localizes to MTOCs and kinetochores (red). By anaphase I, PLK1 accumulates at the spindle midzone.

Kitajima and colleagues first examined the normal localization patterns of PLK1 during meiosis of oocytes using immunostaining and 4D live imaging techniques. PLK1 was initially found dispersed in the cytoplasm during prophase I, and was activated and localized to microtubule organizing centers (MTOCs) before nuclear envelope breakdown (NEBD). When oocytes were treated with an inhibitor to specifically block PLK1 function, there was a marked delay in the timing of NEBD and of chromosome condensation, two events that signal the resumption of meiosis. The resumption of meiosis requires another kinase, CDK1, which is known to be activated by PLK1. Analyses by the researchers indicated that in addition to activating CDK1, PLK1 also regulates NEBD through an alternative route. PLK1 was found to contribute to MTOC formation, and to be required for proper meiotic spindle assembly after NEBD as well.

Inhibiting PLK1 function also caused chromosomal misalignment in during metaphase I. When they investigated the cause of this misalignment, the researchers discovered a reduction in phosphorylation

levels of BUBR1, which is essential for kinetochore function, and an increase in the number of microtubules that were not attached to kinetochores (a region of the chromosome that binds to microtubules). As the PLK1 was seen to localize to the kinetochores after NEBD under normal conditions, their findings suggest that PLK1 stabilizes the binding between kinetochores and microtubules.

Normally, when problems occur in chromosomal alignment, the spindle assembly checkpoint (SAC), a mechanism preventing the onset of anaphase I, is activated thereby preventing oocytes from undergoing transition from metaphase to anaphase. In PLK1-inhibited oocytes, meiosis was arrested at metaphase. Upon closer examination, PLK1 was found to be essential for the degradation of EMI1, a molecule that prevents the APC/C from being activated to push oocyte to enter anaphase. In contrast to what is seen in somatic cell division, inhibiting SAC alone in oocytes does not resume cell division, thus APC/C activation via PLK1 is necessary for progression to anaphase. In addition, their experiments show that even after APC/C is activated and oocytes enter anaphase PLK1 contributes to chromosome segregation, maintaining chromosome condensation, and also cytokinesis.

“The present study shows that PLK1 is an important factor that directs multiple events during oocyte maturation, similar to PLK1 functions in mitosis; but there are also slight differences in its roles and contributions,” says Kitajima. “Our joint research recently uncovered a binding partner of PLK1 called, Meikin, found in the kinetochores of oocytes which regulates meiosis-specific kinetochore function*. Thus, the functions and contributions of PLK1 during meiosis appear to be regulated by factors uniquely assembled by the oocyte.”

* Kim J, et al, *Nature* (2014) doi:10.1038/nature14097