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LS-13-P-3003 Many functions for PLK1 in mammalian oocytes: Nuclear permeabilization, nuclear lamina breakdown, acentriolar spindle assembly and APC/C activation

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Polo-like kinase 1 (PLK1) is a protein kinase that orchestrates multiple events of cell division. Although PLK1 function has been intensively studied in centriole-containing and rapidly cycling somatic cells, little is known about its function in the meiotic divisions of mammalian oocytes, which arrest for a long period of time in prophase before meiotic resumption and lack centrioles for spindle assembly. Here, using specific small molecule inhibition combined with live oocyte imaging, we comprehensively describe PLK1's functions during meiosis in mouse oocytes. We show that PLK1 becomes activated at meiotic resumption on microtubule organizing centers (MTOCs) and kinetochores. We demonstrate a function of PLK1 in nuclear envelope permeabilization and nuclear lamina breakdown during resumption of meiosis. PLK1 is also needed to recruit centrosomal proteins to acentriolar MTOCs to promote bipolar spindle formation, as well as for stable kinetochore-microtubule attachment through BUBR1 phosphorylation. Consequently, PLK1 inhibition leads to metaphase I arrest with misaligned chromosomes activating the spindle assembly checkpoint (SAC). Unlike in mitosis, the metaphase I arrest is not bypassed by the inactivation of the SAC. We show that PLK1 is required for the full activation of the anaphase promoting complex/cyclosome (APC/C) by promoting the degradation of the APC/C inhibitor EMI1 and is therefore essential for entry into anaphase I. Moreover, our data suggest that PLK1 is required for proper chromosome segregation and the maintenance of chromosome condensation during the meiosis I-II transition, independently of the APC/C. Thus, our results define the meiotic roles of PLK1 in oocytes and reveal interesting differential requirements of PLK1 between mitosis and oocyte meiosis in mammals.

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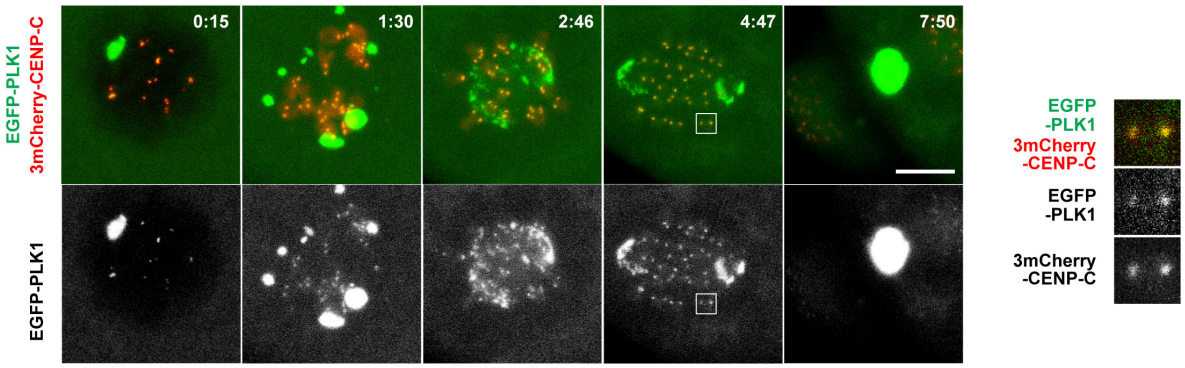

Fig. 1: PLK1 localizes to MTOCs and kinetochores:Time-lapse imaging of meiosis I in oocytes expressing EGFP-PLK1 (green) and 3mCherry-CENP-C (kinetochores, red). Maximum intensity *z*-projection images at representative time points are shown. Time after induction of meiotic resumption (h:mm). Scale bar = 10 µm. Insets show magnified images on kinetochores.

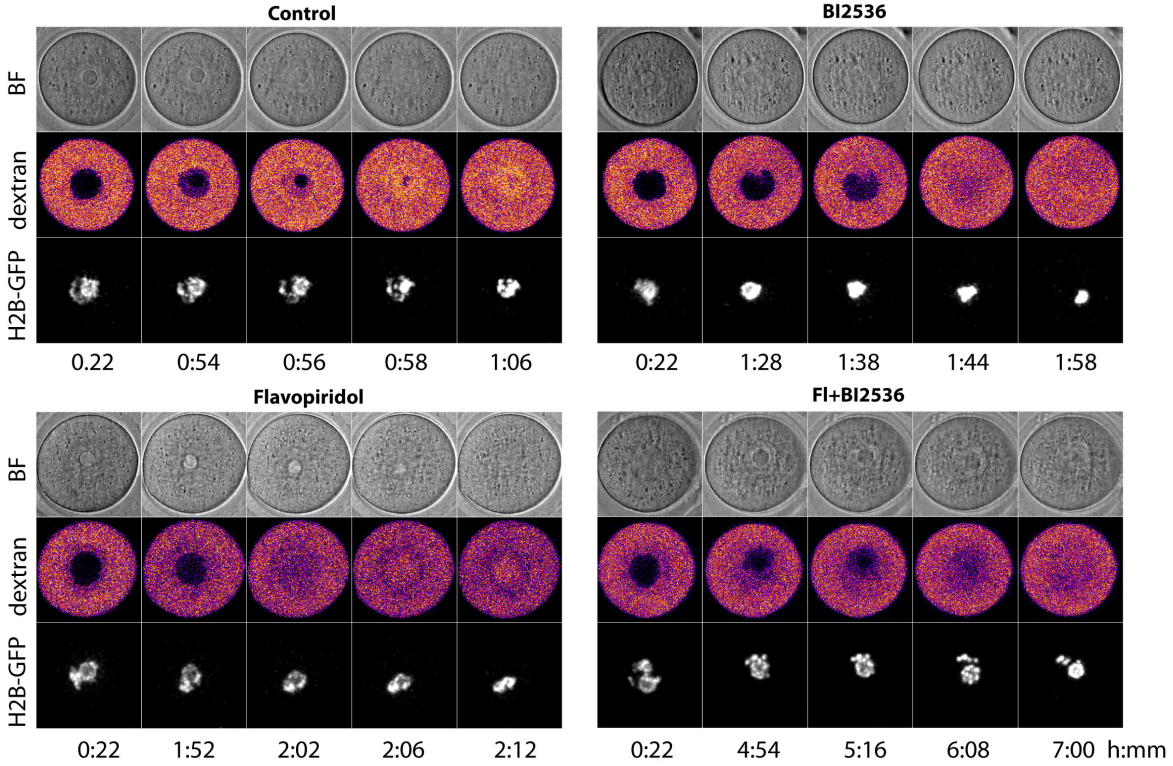

Fig. 2: PLK1 with CDK1 cooperates on NE permeabilization: Time lapse of 70kDa-dextran-TRITC microinjected H2B-EGFP oocytes after induction of meiotic resumption in control, BI2536-, flavopiridol (Fl) and Fl+BI2536 medium. 70kDa-TRITC signal is pseudocolored and maximum intensity *z*-projection for H2B-EGFP is gray.