Antibody microinjection reveals an essential role for human polo-like kinase 1 (Plk1) in the functional maturation of mitotic centrosomes

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Mammalian polo-like kinase 1 (Plk1) is structurally related to the polo gene product of Drosophila melanogaster, Cdc5p of Saccharomyces cerevisiae, and plo1+ of Schizosaccharomyces pombe, a newly emerging family of serine-threonine kinases implicated in cell cycle regulation. Based on data obtained for its putative homologues in invertebrates and yeasts, human Plk1 is suspected to regulate some fundamental aspect(s) of mitosis, but no direct experimental evidence in support of this hypothesis has previously been reported. In this study, we have used a cell duplication, microinjection assay to investigate the in vivo function of Plk1 in both immortalized (HeLa) and nonimmortalized (Hs68) human cells. Injection of anti-Plk1 antibodies (Plk1+) at various stages of the cell cycle had no effect on the kinetics of DNA replication but severely impaired the ability of cells to divide. Analysis of Plk1(+)-injected, mitotically arrested HeLa cells by fluorescence microscopy revealed abnormal distributions of condensed chromatin and monoastral microtubule arrays that were nucleated from duplicated but unseparated centrosomes. Most strikingly, centrosomes in Plk1(+)-injected cells were drastically reduced in size, and the accumulation of both gamma-tubulin and MPM-2 immunoreactivity was impaired. These data indicate that Plk1 activity is necessary for the functional maturation of centrosomes in late G2/early prophase and, consequently, for the establishment of a bipolar spindle. Additional roles for Plk1 at later stages of mitosis are not excluded, although injection of Plk1+ after the completion of spindle formation did not interfere with cytokinesis. Injection of Plk1+ into nonimmortalized Hs68 cells produced qualitatively similar phenotypes, but the vast majority of the injected Hs68 cells arrested as single, mononucleated cells in G2. This latter observation hints at the existence, in nonimmortalized cells, of a centrosome-maturation checkpoint sensitive to the impairment of Plk1 function.
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