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pararota checaes a kinesin like protein required to organize the central spindle and contractile ring for cytokinesis

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Mutations in the *Drosophila* gene pavarotti result in the formation of abnormally large cells in the embryonic nervous system. In mitotic cycle 16, cells of pav mutant embryos undergo normal anaphase but then develop an abnormal telophase spindle and fail to undertake cytokinesis. We show that the septin Peanut, actin, and the actin-associated protein Anillin, do not become correctly localized in pav mutants. pav encodes a kinesin-like protein, PAV-KLP, related to the mammalian MKLP-1. In cellularized embryos, the protein is localized to centrosomes early in mitosis, and to the midbody region of the spindle in late anaphase and telophase. We show that Polo kinase associates with PAV-KLP with which it shows an overlapping pattern of subcellular localization during the mitotic cycle and this distribution is disrupted in pav mutants. We suggest that PAV-KLP is required both to establish the structure of the telophase spindle to provide a framework for the assembly of the contractile ring, and to mobilize mitotic regulator proteins.

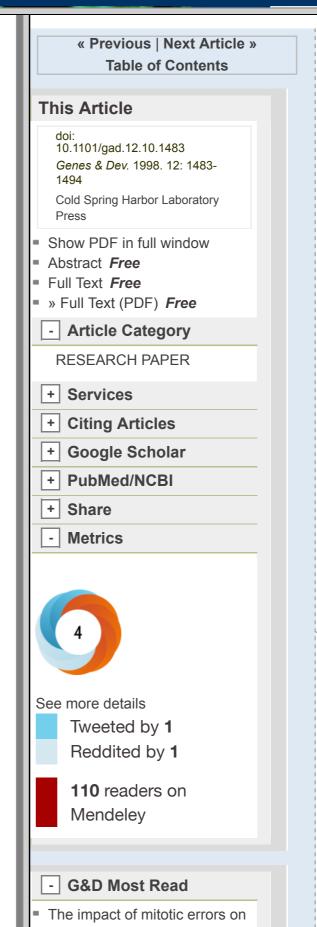
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Cytokinesis is the ultimate act of mitosis, whereby segregated daughter nuclei are partitioned into two separate cells. In eukaryotes, this is accomplished by an actinmyosin contractile ring that forms around the cell equator during mitosis and constricts inwards at telophase (Schroeder 1972). In higher eukaryotes the correct positioning and assembly of the contractile ring requires the mitotic spindle, although the mechanism by which this occurs is a matter of controversy (Swann and Mitchison 1956; Zhang and Nicklas 1996). The classical experiments of Rappaport (1961) suggest that the spindle poles are sufficient to stimulate cytokinesis. By generating horseshoe-shaped single cell echinoderm embryos containing two mitotic spindles, not only were cleavage furrows formed in the central region of the mitotic spindles, but an extra furrow was formed equidistant between two asters lacking any intervening chromosomes or spindle microtubules. Similar phenomena have been observed in cultured mammalian cells, and although this does occur

first model, the poles signal directly to the equatorial cortex of the cell, perhaps by the action of astral microtubules (Devore et al. 1989). Alternatively, the astral relaxation model (White and Borisy 1983) proposes that spindle poles induce a relaxation of the cell cortex nearest to the poles, leading to a tension differential between the poles and the equator that results in equatorial contraction. However, this model has been discredited recently by force measurements showing that tension increases at the equator without a concomitant decrease at the cell poles (Burton and Taylor 1997).

On the other hand, there is growing evidence that the central spindle plays an essential role in the positioning and assembly of the contractile ring. The central spindle is composed of a dense network of overlapping antiparallel microtubules that forms between the separating daughter nuclei during anaphase (Mastronarde et al. 1993). In cultured cells induced to develop multipolar spindles as result of treatment with low concentrations





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