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Flies stretch their cells to avoid a chromatin trap

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Successful mitosis requires the spatiotemporal coordination of chromosomal and cytoskeletal events. The mitotic cell has evolved a series of surveillance mechanisms to guarantee the fidelity of cell division and avoid aneuploidy (Holland and Cleveland, 2009). These mitotic checkpoints act at specific stages of the cell cycle to ensure that everything goes according to plan before proceeding to the next stage.

One of these crucial points is the moment in which the cell splits up in two through the process of cytokinesis, the final stage of cell division (Eggert et al., 2006). The initial step in cytokinesis is the localization of myosin at the equatorial cortex, followed by the formation of an actomyosin ring. When this contractile ring closes it also drives the furrowing of the cytoplasmic membrane at the cell equator, compressing the cytoplasm and the midzone microtubules into the midbody. But before the process goes any further, the cell has to check that chromosome segregation has occurred normally and that the midzone is clear of chromatin. If cytokinesis proceeded in the presence of a chromatin bridge, it could result in a negative outcome for the cell: chromosome breakage would generate aneuploidy and cytokinesis failure would lead to tetraploidy. In either case, the consequences would be potentially deleterious. For this reason, the mitotic cell delays abscission, the last stage of cytokinesis (Neto and Gould, 2011), until the chromatin bridges have been resolved: this is called the abscission checkpoint. In recent years, work in yeast, Drosophila melanogaster, and mammalian cells has contributed to a better understanding of the abscission checkpoint and its regulation by Aurora B kinase (Carmena, 2012). Aurora B is the enzymatically active component of the chromosomal passenger complex (CPC), an essential protein complex that performs multiple regulatory roles in mitosis and cytokinesis (Carmena et al., 2009; van der Waal et al., 2012). The CPC component Borealin interacts with Shrb/CHMP4C, a subunit of ESCRT-III, a protein complex responsible for the scission activity. The pathway is not totally conserved: in human cells, Aurora B acts through phosphorylation CHMP4C, but in Drosophila it seems that Borealin acts in the regulation of abscission in an Aurora-independent way.

In this issue, Kotadia et al. describe a novel mechanism by which animal cells deal with exceptionally long chromatid arms in late mitosis. Drosophila larval neuroblasts elongate during anaphase and telophase to allow chromatin to clear the midzone before cytokinesis proceeds. Drosophila larval neuroblasts divide asymmetrically into a smaller ganglion mother cell (GMC) and a neuroblast (NB). To generate long chromatids, the authors induced double-strand DNA breaks in the ribosomal DNA of the X chromosome by induction of the I-CreI endonuclease. The resulting chromosomes fragments remain linked by a DNA tether that increases chromatin tid (Royou et al., 2010). Using this system, the authors observed that the asymmetrically dividing neuroblasts changed their usual spherical shape, becoming transiently elongated to accommodate the longer chromatin arms. Interestingly, the asymmetry of the division itself was not affected, although the shape change was more noticeable in the GMC, which became almost tubular compared with the neuroblast. The mitotic spindle appeared slightly more elongated and shifted toward the GMC. Most noticeably, although myosin localized to the equator, it did...
Conversely if the pathway is indeed conserved, it will be worth exploring how it is integrated with other mechanisms that regulate abscission. In particular a most intriguing question for future research will be how this new pathway is coordinated with the previously described Aurora B–dependent pathways. Aurora B kinase has not only been shown to have a key function in the regulation of abscission, but also has a role in the regulation of contractile ring assembly (Lewellyn et al., 2011) and furrow ingression. Aurora B regulates RhoA activity indirectly in different ways (Minoshima et al., 2003; Birkenfeld et al., 2007; Touré et al., 2008) and modulates the binding of myosin to the cytoskeleton (Ozlü et al., 2010), so it will be intriguing to investigate if this essential mitotic kinase contributes in any way to this new pathway.

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