RESEARCH HIGHLIGHTS

Adjusting kinetochore–microtubule attachments

Stringent control of the events at the kinetochore–microtubule interface is critical for faithful chromosome segregation. Compton and colleagues now report how a switch in CLASP1-binding partners at the outer kinetochore fine-tunes microtubule attachment during the transition from prometaphase to metaphase (*EMBO J.* doi:10.1038/emboj.2010.230).

The authors initially find that the microtubule and kinetochore protein astrin enhances the stability of kinetochore microtubules in metaphase, but not in prometaphase, which is opposite to the known role of the kinesin Kif2b. They show that the localization of astrin and Kif2b on kinetochores is mutually exclusive and that astrin depletion causes persistent Kif2b kinetochore association. The outer kinetochore and microtubule-associated protein CLASP1 is required for the kinetochore localization of both proteins, but binds astrin and Kif2b in independent complexes. Kif2b–CLASP1 is also shown to generate a poleward force at kinetochores; this is known to be important for chromosome movement in prometaphase.

Thus, the authors present a model where, in early mitosis, Kif2b–CLASP1 promotes kinetochore–microtubule dynamics, correction of erroneous attachments and chromosome movement, while the later recruitment of astrin–CLASP1 stabilizes kinetochore microtubules and promotes chromosome alignment and silencing of the spindle assembly checkpoint. Interestingly, a role for an astrin–SKAP complex in maintaining chromosome alignment is also reported by Cheeseman and colleagues (*J. Cell Biol.* doi:10.1083/jcb.201006129). Furthermore, the work of both the Compton and Cheeseman groups show that Aurora B has a critical role in regulating the recruitment of an astrin-containing complex to kinetochores. CKR

Neutral drift in intestinal stem cells

Homeostasis in the mammalian intestinal epithelium relies on the presence of a fixed number of stem cells with self-renewing capacity and the ability to generate progenitors that differentiate into the various cell types that constitute a crypt. The Clevers and Winton groups use individual cell fate mapping and quantitative modelling to provide support in favour of a stochastic model of intestinal stem cell (ISC) self-renewal in which stem cell numbers are maintained at the level of the whole population (*Cell* 143, 134–144 (2010); *Science* doi:10.1126/science.1196236).

Clevers and colleagues combine a randomly inducible multi-colour reporter system that allows labelling of cells and mapping of their progeny with a mouse strain expressing the fluorescently labelled stem cell marker Lrg5. Short-term clonal analysis revealed that division of ISCs can give rise to two ISCs, one ISC and one progenitor, or two progenitors. Thus, ISC can adopt divergent fates, an observation that contrasts with the hierarchical view of asymmetric stem cell division, which invariably generates one stem cell and one progenitor. Using long-term lineage tracing, both studies observe a drift towards monoclonality over time, which translates into all stem- and differentiated-cells of a crypt deriving from a single original stem cell; mathematical modelling suggests that ISCs adopt neutral drift dynamics. In this stochastic model, however, the fate of ISC progeny may be influenced by the available contacts with Paneth cells, a specialized cell type in the crypt that has been proposed to provide signals required for ISCs maintenance. NLB

Calcium activates Aurora-A kinase

The Aurora-A kinase (AurA) is essential for normal mitotic progression, but accumulating evidence suggests that it has important biological functions during interphase as well. However, the mechanism by which AurA is activated in interphase cells remains elusive. Golemis and colleagues now report that calcium–calmodulin (CaM) binding activates AurA during interphase (*Nat. Commun.* doi:10.1038/ncomms1061).

Increases in intracellular calcium concentration in interphase cells led to rapid autophosphorylation and activation of AurA. This effect was independent of the AurA binding partner NEDD9 — which is important for AurA activation in mitosis — but instead dependent on CaM. A direct interaction between AurA and CaM was confirmed *in vitro* and *in vivo*, and the minimal interaction domain was mapped to the AurA amino terminus.

Active AurA has been detected at the basal body of cilia, where it regulates ciliary resorption. In cancerous cells, dysregulated activation of AurA is associated with aneuploidy. It will be important to determine whether calcium-mediated activation of AurA is important in these contexts, and elucidate if CaM binding affects the mitotic function of AurA. EJC

Myosin II muscles in on asymmetric cell division

Cells can divide asymmetrically, giving daughter cells that have distinct fates. In many cells asymmetrical division is determined by the positioning of the mitotic spindle, which is pulled towards one end of the cell. Division occurs in the middle of the misplaced spindle, resulting in two differently sized daughter cells. Using fluorescence markers and live-cell imaging, Ou *et al.* show that asymmetric division occurs in some *Caenorhabditis elegans* Q neuroblasts even though the centrosomes of the spindle are initially located equidistant from the centre of the cell (*Science* doi:10.1126/science.1196112). In these cells, cortical GFP–myosin II was distributed unevenly, with more accumulating on the anterior side of the cell. As a result this side of the cell is squeezed, which pushes cytoplasm to the posterior side of the cell, causing expansion, and eventually asymmetric division. The authors destroyed myosin function by laser irradiation of GFP–myosin II, which produces hydroxyl radicals that damage the protein. This reduced asymmetric division, and led to greater survival of the anterior daughter cells, which otherwise underwent apoptosis. The authors demonstrate that myosin polarization has an important role in asymmetric division of cells that can also affect subsequent cell survival, differentiation and fate. GD

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