Cells polarize contractility to move together

During *Drosophila melanogaster* oogenesis, border cell clusters detach from the follicular epithelium of the egg chamber and migrate collectively towards the oocyte. Although collective cell migration requires polarized actomyosin contractility, the mechanisms regulating this process are not fully elucidated. Majumder *et al.* now show that the Par-1 cell polarity kinase spatially controls myosin-II (Myo-II) activity for correct border cell migration (*Curr. Biol.* **22,** 363–372; 2012).

Par-1 was previously shown to impair border cell protrusions and detachment from the epithelium. The authors observed similar defects in border cell clusters deficient for Myo-II, and established that Par-1 increases the levels of active Myo-II in border cells. This was shown to occur indirectly through the Par-1-mediated phosphorylation and inactivation of myosin phosphatase, which normally inhibits Myo-II. Par-1 is known to localize to the rear of the border cell cluster. This spatial restriction was shown here to result in local inhibition of myosin phosphatase and a concurrent increase of Myo-II activity at the same site. The authors propose that the Par-1-mediated spatial enhancement of Myo-II activity and subsequent polarized cell contraction are crucial for cell detachment and collective migration. These findings link cell polarity to the control of actomyosin contractility, and shed light on the regulatory networks influencing collective cell migration. AIZ

Telomeric damage after mitotic arrest

Chromosome ends need to be protected from DNA-damage signalling and repair pathways to avoid aberrant repair events. However, senescence or loss of components of the so-called shelterin complex causes induction of a DNA-damage response at telomeres. Karlseder and colleagues now discover that prolonged mitotic arrest can also result in the formation of telomeric DNA-damage foci (*Nat. Struct. Mol. Biol.* **19,** 387–394; 2012)

The authors discovered that introducing prolonged mitotic arrest by interfering with sister chromosome cohesion (by depletion of the cohesin subunit RAD21, sororin or shugoshin) or the mitotic spindle (by microtubule-targeted drugs or inhibition of the Eg5 kinesin), leads to an increase in telomere-associated DNA damage. The prolonged mitotic arrest was associated with the loss of telomeric 3′ overhangs and activation of the ATM kinase, similarly to what is observed after inactivation of the DNA repair protein TRF2. Indeed, TRF2 was reduced at telomeric repeats, and its forced expression reduced the formation of telomeric DNA-damage foci. Colcemid-treated cells, which were then released to allow mitosis to proceed, showed persistent foci in G1, leading to p53 activation and G1 phase arrest. Although it remains unclear exactly how prolonged mitotic arrest causes the removal of TRF2, the authors could show that the mitotic kinase Aurora B, but not the spindle assembly checkpoint, is required.

One implication of these results is that therapeutic drugs that induce mitotic arrest may ultimately cause aneuploidy due to telomeric deprotection. CKR

A tale of two mTORCs

The kinase mTOR exists as part of two different complexes, mTORC1 and mTORC2, each with distinct roles. mTORC1 regulates cell growth and differentiation, whereas mTORC2 modulates insulin signalling. Inhibition of mTORC1 is well known to promote longevity; indeed, rapamycin, a drug thought to specifically inhibit mTORC1, increases lifespan in many species. However, rapamycin treatment can also induce glucose intolerance and insulin resistance. Sabatini, Baur and colleagues resolve this paradox by showing that rapamycin also inhibits mTORC2 function (*Science* **335,** 1638–1643; 2012).

Rapamycin treatment in mice promoted expression of gluconeogenic genes and altered glucose homeostasis. These mice eventually developed insulin resistance. Intriguingly, genetic ablation of mTORC2, but not mTORC1, also led to defects in glucose homeostasis and insulin resistance. Rapamycin treatment inhibited phosphorylation of mTORC2 substrates, indicating that rapamycin blocks the activity of both mTORC1 and mTORC2. The authors went on to show that mice heterozygous for certain mTORC1 components had an increased lifespan but normal glucose tolerance and insulin sensitivity.

These findings support the hypothesis that enhanced longevity can be achieved without defects in glucose homeostasis by specifically targeting the mTORC1 complex. The presumption that rapamycin is a specific mTORC1 inhibitor will also have to be reconsidered in light of these data. EJC

Kinesin-1 prevents premature pronuclei encounter

In many organisms, the female centrioles are degraded in oocytes and the zygote centrosome is inherited from the sperm. Fertilization often proceeds before completion of female meiosis II, and therefore capture of the female DNA by the male centrosomal aster has to be delayed until after completion of this division. McNally and colleagues (*Dev. Cell* http://doi.org/htm; 2012) have found that, in *Caenorhabditis elegans*, the motor protein kinesin-1 and its associated binding protein KCA-1 coat the male pronucleus and centrioles to prevent the recruitment of the maternal pericentriolar material required for centrosome maturation. They observe that RNA-interference depletion of the kinesin-1 motor chain, the kinesin light chain or KCA-1 induces the premature growth of microtubules by the sperm aster and the capture of the female spindle by the sperm centrosome. Using immunofluorescence, the kinesin motor and KCA-1 were shown to localize tightly around the male pronucleus in a region devoid of yolk proteins. This coating decreases after meiotic completion, and correlates with the degradation of KCA-1 protein in an anaphase-promoting complex (APC)-dependent manner. This function of kinesin-1 is independent of microtubules, and thus does not seem to require kinesin-1 motor activity. The authors also uncover a further role for kinesin-1 in positioning the male pronucleus deep inside the cytoplasm until completion of female meiosis near the cortex. NLB

By Emily J. Chenette, Christina Karlsson Rosenthal, Nathalie Le Bot and Alexia-Ileana Zaromytidou

© 2012 Macmillan Publishers Limited. All rights reserved