Lengthening without letting go

Merotelic chromosome attachments present the cell with a particularly threatening scenario. With a single kinetochore attached to both spindle poles, the tension on this kinetochore ensures that no error message is sent out, as would be the case with a detached kinetochore. Most researchers presumed that the relatively lower tension on the “incorrect” attachment (the one that is relieved by the codirectional pull on the singly attached sister kinetochore) ensures detachment of that connection, followed by attachment to the correct pole.

But now Daniela Cimini, Lisa Cameron, and Ted Salmon (University of North Carolina, Chapel Hill, NC) show that this detachment process rarely makes it to completion. Instead, a tension-dependent elongation of the incorrect attachment allows the chromosome to reach the correct side during anaphase.

The group first determined that only 8 out of 54 merotelic attachments were corrected during metaphase. This may not be surprising—the likelihood of all kinetochore microtubules letting go at one time is presumably very low, and newly released sites will often still be oriented toward and thus reattach to the incorrect pole. The tension differential did, however, result in more microtubules attaching to the correct rather than incorrect pole for most merotelic situations.

Once anaphase began, this difference was crucial. With the sister kinetochore departed for its pole, the merotelic kinetochore experienced the same force at both of its attachments. But the incorrect attachments, with fewer microtubules, experienced greater tension per microtubule as the spindle poles separated. Microtubule polymerization rate is thought to be proportional to tension, which would explain why the thinner microtubule bundles got relatively much longer. This put the chromosomes on the side of the spindle where they needed to be. Thus, says Cimini, “you get correct chromosome segregation without [fully] correcting the error of microtubule attachment.”

Reference: Cimini, D., et al. 2004. Curr. Biol. 14:2149–2155.

The oenocytes went 3 by 3

A specialized cell type in flies leaves its specifying hub in groups of 3 cells, according to Véronique Brodou, Philip Elstob, and Alex (NIMR, Mill Hill, London, UK). Each group gets stimulation of its EGF receptor (EGFR) in a controlled pulse, which may ensure reliable differentiation.

Gould studies oenocytes—a large, secretory cell type in flies that may generate or respond to hormone signals during embryonic moults. Looking at oenocyte specification in real time, Gould’s group noticed that cells clustered around a C1 cell—the source of EGFR ligand—in groups of 3, and departed in the same cohorts. Normal animals went through two such pulses of 3 cells arriving and leaving, although overexpression of an EGFR ligand resulted in up to 7 or 8 pulses.

Several downstream targets of EGFR signaling were expressed in far more than the 3 cells immediately around each C1. But the London group found that other critical targets were expressed only in the 3 closest cells thanks to the feedback inhibitor Argos, which turns off signaling in more distant cells receiving intermediate or low levels of EGFR stimulation. Interference with the Argos system eliminated the 3 by 3 nature of the specification process, and resulted in late defects in differentiation.

The grouping of 3 cells per round appears to reflect the geometry of cell packing: that is how many cells fit around a single C1 cell. Argos then ensures that cells further away register no signal rather than a half-hearted signal that might lead to errors. “By delaminating in a pulse-by-pulse mechanism,” says Gould, “it would provide you with a way of regulating exposure to ligand in a more reproducible and regulated manner.” The pulsatile strategy may be used in other signaling systems such as the fly eye, where EGFR stimulation drives stepwise differentiation of photoreceptors.

Reference: Brodou, V., et al. 2004. Dev. Cell. 7:885–895.