expression of Vdac2 inhibited tBid-induced apoptosis of *Bax*$^{-/-}$ cells, but not *Bak*$^{-/-}$ cells, which indicates that Vdac2 negatively regulates Bak-dependent apoptosis.

Cells deficient for Vdac2 were far more sensitive to death stimuli than *Vdac1*$^{-/-}$ and *Vdac3*$^{-/-}$ cells, both of which had similar sensitivities to wild-type cells. By re-expressing Vdac2, the susceptibility to apoptosis of *Vdac2*$^{-/-}$ cells reverted to normal. So, Vdac2 has a physiological role that is distinct from the other Vdac isoforms.

When analysing the apoptosis phenotype of *Vdac2*$^{-/-}$ cells, the authors noted an increased loss of mitochondrial transmembrane potential and the accelerated release of cytochrome *c*, compared with wild-type cells. After treatment with death stimuli, *Vdac2*$^{-/-}$ cells showed caspase activity and Bak oligomerization earlier than wild-type cells.

The authors concluded that Vdac2 is a specific inhibitor of Bak-dependent mitochondrial apoptosis, which, when absent, causes increased susceptibility to apoptotic death.

Arianne Heinrichs

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promoters close to an LTR were de-repressed (that is, unsilenced) in cells that lacked these RNAi-pathway components.

Further experiments showed that — at least for the two genes that were studied — RNAi-dependent modifications at LTRs mediate transcriptional repression, and removal of these LTRs leads to constitutive expression (de-repression) of the adjacent genes. Taken together, these results indicate that LTRs are needed to silence meiotically induced genes during vegetative growth. More generally, the authors conclude that LTRs can act as developmental effectors through the RNAi pathway, restricting the expression of a gene to a distinct differentiation pathway.

These fascinating results in fission yeast show that despite the recent flurry of RNAi research activity in a plethora of models, we still have a way to go before we fully understand this process. After Schramke and Allshire's study, the role of repetitive DNA elements in RNAi in other models is likely to be the focus of many new studies.

Nick Campbell, Associate Editor,
Nature Reviews Genetics

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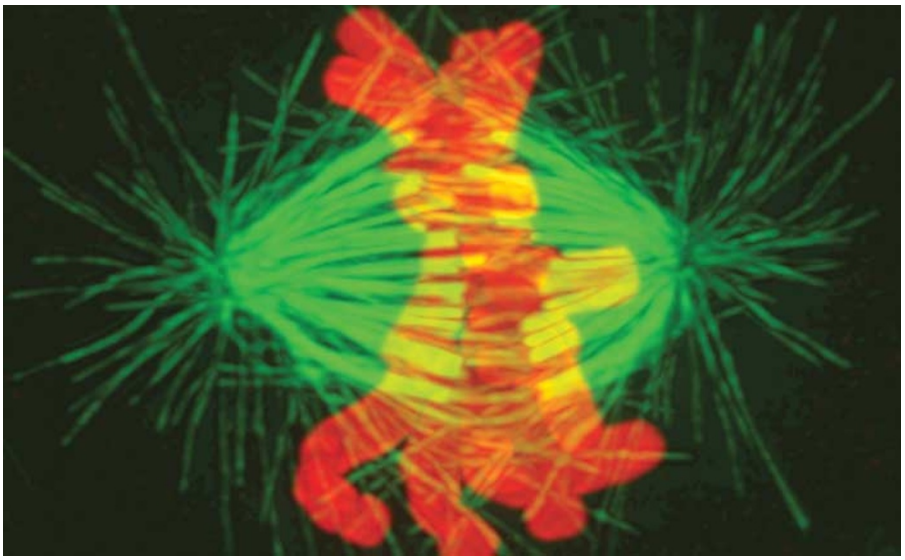

CYTOKINESIS

Right place, right time

The symmetrical arrangement of chromosomes and the mitotic spindle during metaphase creates an obvious point for initiating cell cleavage and ensures that the mother cell divides equally and symmetrically. It has previously been suggested that the spindle microtubules themselves play an integral part in choosing the cell-division plane and initiating cleavage-furrow formation.

In a recent report in *Nature*, Julie Canman and colleagues challenge the widely held view that the symmetrical bipolar spindle is required for cleavage-site formation. In an elegant set of experiments, they used a small-molecule inhibitor to block the kinesin Eg5, which is essential for establishing a bipolar spindle. As this inhibition activated the spindle checkpoint, they blocked this checkpoint as well.

What they found was that monopolar half-spindles formed, but that furrow formation and cytokinesis still occurred. The cell-division plane formed on the side of the cell facing the chromosomes and not at the poles. So, these results showed that two opposing microtubule arrays are not essential for cell division.

The authors then imaged fluorescently-tagged tubulin to monitor the dynamics of microtubules inside bipolar and monopolar cells undergoing cytokinesis. They noticed that a stable subpopulation of microtubules was associated with the cytokinetic furrows. These stable microtubules were associated with chromosomes, and only formed on the side of the asymmetric monopolar spindles that were associated with chromosomes, in the same place as the site of furrowing. Dynamic microtubules populated the cell poles, presumably acting to inhibit furrow formation outside of the cell equator.

The authors propose a model whereby, at least in some cultured mammalian cells, chromosomes form connections with the cell cortex through as-yet-undetermined microtubule stabilization factors. These stable microtubules then signal directly to the neighbouring cell cortex to form a furrow in their vicinity, and might act as tracks for motor proteins to deliver regulators and components of the cytokinetic furrow to the cell cortex.

In non-mammalian cells, it has also been unclear which part of the spindle apparatus is responsible for furrow positioning. Alsop and Zhang now report, in *The Journal of Cell Biology*, the systematic dissection of the role of each structural component.

Using micromanipulation, the authors removed asters and chromosomes from grasshopper spermatocytes in metaphase, leaving microtubules as the only structural constituent. This resulted in the disassembly of the spindle and, subsequently, the assembly of microtubule bundles. At first, the microtubules radiated towards the cell cortex; later, they underwent transient formations of bipolar and monopolar pseudospindles; and, ultimately, they formed disorganized arrays of bundled microtubules.

Induction of furrow initiation occurred at midzones of sustained bundles of microtubule arrays. Often, furrow induction occurred at multiple locations, but many furrows were transient and regressed. Furrow initiation and cytokinesis were delayed, however, probably because of microtubule reorganizations. So, Alsop and Zhang concluded that microtubules — regardless of their order or symmetry in the spindle — are sufficient to induce cell cleavage, reinforcing the idea that the microtubules themselves ensure that cells divide equally and symmetrically.

Mirella Bucci, Associate Editor, Nature

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