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CELL DIVISION

Time to bud off

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URLs

Ase1
http://ca.expasy.org/uniprot/P50275

Ndc10
http://ca.expasy.org/uniprot/P32504

Ndc80
http://db.yeastgenome.org/cgi-bin/locus.pl?locus=ndc80

Ipl1
http://ca.expasy.org/uniprot/P38991

Boi1
http://ca.expasy.org/uniprot/P38041

Boi2
http://ca.expasy.org/uniprot/P39969

Cytokinesis, the final step in cell division, is when two daughter cells become physically dissociated. How cytokinesis is coordinated with the preceding step, anaphase, during which chromosome segregation takes place, has been unclear. Reporting in *Cell*, Barral and colleagues have identified a signalling pathway — called NoCut — that delays the completion of cytokinesis by cell cleavage (also known as abscission) in budding yeast cells with spindle-midzone defects.

Chromosome segregation is supported by the so-called spindle midzone, which contains numerous components, including the microtubule-bundling protein Ase1. In animal cells, spindle-midzone defects lead to cytokinesis failure. To test whether the spindle midzone is required for cytokinesis in budding yeast, Barral and co-workers compared dividing wild-type and *ase1*Δ cells, and noted that a greater fraction of mutant cells underwent membrane contraction ('pinching' of the bud neck) but not abscission. Conditional *ase1* mutant cells formed chains that failed to separate. Mutants of other spindle-midzone components, such as the kinetochore proteins Ndc10 and Ndc80 (which are important for spindle-midzone stability), also had cytokinesis defects. Together, these findings indicate that the spindle midzone is required for proper abscission.

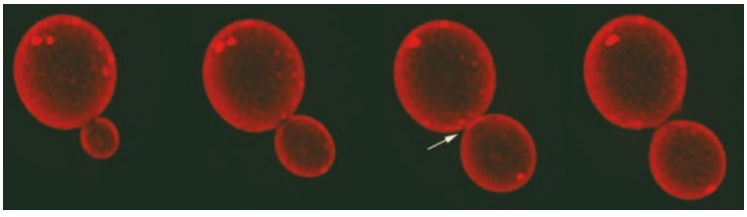
The authors hypothesized that if abscission is inhibited in response to a defective spindle midzone, then inhibition-defective cells should complete abscission even in the absence of a functional spindle midzone. Barral and colleagues tested whether inactivation of the spindle-midzone protein Aurora kinase Ipl1, which does not cause a cytokinesis defect, could rescue cytokinesis in midzone-defective cells. This was indeed the case, so a complete spindle midzone is not absolutely required for cytokinesis and midzone defects cause the Ipl1-dependent inhibition of abscission.

As Ipl1 was never observed at the bud neck, the authors postulated that Ipl1 inhibits abscission through proteins that shuttle between the nucleus and the bud neck, as is the case for the anillin-related proteins Boi1 and Boi2. Cells of the *ndc10-1 boi1*Δ *boi2*Δ triple-mutant strain underwent normal abscission despite the spindle-midzone defect, indicating that, like Ipl1, Boi1 and Boi2 have a role in the inhibition of abscission. In *ipl1*-mutant cells, Boi1 and Boi2 remained nuclear during the entire cell cycle and failed to localize to the bud neck of anaphase cells. This indicates that Ipl1 is required for the proper localization of Boi1 and Boi2, which both function downstream of Ipl1.

To investigate the physiological role of Boi1 and Boi2 in cytokinesis, Barral and colleagues analysed the progression of cytokinesis in wild-type and *boi1*Δ *boi2*Δ double-mutant cells. The interval between membrane contraction and resolution was significantly reduced in the double-mutant cells compared with the wild-type cells. In *ase1*Δ cells with a defective spindle midzone, this interval was extended compared with wild-type cells. This delay depended on Boi1 and Boi2, as Ase1-depleted cells that were also defective for Boi1 and Boi2 completed cytokinesis with the kinetics of wild-type cells. This implies that Boi1 and Boi2 control the timing of abscission in wild-type cells and delay abscission in response to spindle-midzone defects.

So the authors have identified a signalling pathway that represents a cell-cycle checkpoint, which represses cytokinesis in response to defects in the preceding anaphase step. So why is such a checkpoint required? The Barral team shows that the inhibition of abscission in the presence of spindle-midzone defects prevents chromosome breakage during cytokinesis and therefore has a crucial role in maintaining the integrity of the genome.

Arianne Heinrichs



A three-dimensional reconstruction of a wild-type cell during the cell cycle that is labelled with a plasma-membrane marker. The arrow marks the time just before abscission when the plasma membrane is pinched but not yet resolved. Image courtesy of C. Norden, Swiss Federal Institute of Technology in Zurich (ETHZ), Switzerland.

ORIGINAL RESEARCH PAPER Norden, C. *et al.* The NoCut pathway links completion of cytokinesis to spindle midzone function to prevent chromosome breakage. *Cell* **125**, 85–98 (2006)