So what triggers the increased rate of retraction that underlies contraction? Sheetz and colleagues suggest that a molecule hitches a ride on the retreating actin filaments, from the front of the lamellipodium to the rear, signalling contraction when it gets to the back. The authors find that α-actinin and myosin-light-chain kinase (MLCK) are transported in this way, reaching the back of the lamellipodium in around 25 seconds in normal lamellipodia. They propose that MLCK could be a contraction-triggering signal, as inhibiting this enzyme significantly reduced the duration of, or even eliminated, the extension–contraction phase.

Now we need to know why cells behave in this way on tough substrates — is it, as Sheetz and coworkers suggest, that regular periods of contraction enable the locally protruding cell edge to get a better grip on the surface, allowing greater extension towards rigid regions? Is MLCK indeed a signal that triggers squeezing? And could the directed movement of signals along cytoskeletal filaments occur in other contexts, too?

Amanda Tromans

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CELL GROWTH

Testing the water

If you were looking for a mate, how would you find one? The budding yeast *Saccharomyces cerevisiae* has a simple solution. It forms mating projections — polarized cell-surface structures that are involved in cell–cell recognition — that allow it to search for a partner. These projections normally grow towards cells of the opposite sex by responding to pheromone gradients, but when pheromone levels are high, periodic growth occurs in random directions. Bidlingmaier and Snyder now suggest that this allows yeast to 'test the water' to find nearby mating partners in the absence of a pheromone gradient. And, they show that the actin-polymerizing polarisome complex and the Rho-related GTPase Cdc42 regulate this process.

Yeast cells were treated with high concentrations of the α-factor pheromone, which induces periodic mating projections, and were observed by time-lapse photography. When a new projection appeared, the existing projections ceased to grow, which indicates that these two processes are closely linked. So, as the actin cytoskeleton is involved in polarized growth, the authors blocked actin polymerization — and hence the growth of the mating projections — by briefly treating the cells with an actin-polymerization inhibitor. Transient disruption of the actin cytoskeleton produced new projections in the treated cells, which confirmed that termination and initiation of projection growth are tightly linked. But what controls this process?

The polarisome complex, which comprises Spa2, Pea2, Bni1and Bud6, is important for polarized growth. Spa2 has been implicated in the periodic initiation of polarized growth, so the authors investigated whether the proteins of the polarisome complex regulate mating projection. Projections were formed less frequently and were wider, and faster growing, in *spa2*Δ, *pea2*Δ and *bni1*Δ, but not *bud6*Δ, mutants compared with wild-type cells, which indicates that Spa2, Pea2 and Bni1 are involved in controlling the timing and frequency of mating-projection formation. The authors were surprised to find that growth termination was delayed in the *spa2*Δ, *pea2*Δ and *bni1*Δ mutants, which indicates that these proteins are also required to terminate growth.

As Bni1 is a downstream effector of the Cdc42 GTPase, the authors next investigated components of the Cdc42 signalling pathway. They found that Cdc42 and its regulators Cdc24 and Bem3 also control the frequency of projection formation. Interestingly, Bem3 did not affect growth termination, which indicates that initiation and termination might be regulated by distinct, but overlapping pathways. The lack of Fus1 — a protein required for mating — inhibited growth termination, but not growth initiation, providing further evidence that the pathways are partially separated.

The authors propose that Cdc42 phosphorylation activates Bni1 in the polarisome complex, which then promotes projection initiation and, at the same time, terminates the growth of existing projections. As Bem3 and Fus1 only affect part of this process, at least one other regulatory pathway must exist. Many biological processes involve cell polarization, so it will be interesting to see if the proposed mechanism is a general one.

Emma Croager

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WEB SITE

Michael Snyder's laboratory: http://www.yale.edu/snyder/