is the possibility that agents used to initiate the activation of SOCs (for example, depletion of Ca^{2+} in the endoplasmic reticulum by thapsigargin) cause a change in membrane tension which, in turn, activates TRPC1.

The two studies discussed here have significantly advanced our knowledge and thinking about the nature of mechanosensitive channels and the function of non-selective cation channels of the TRP family. However, in looking back on the investigations of TRP channels over the past 10 years, it is salient to note that these studies have involved numerous surprises. Constant vigilance, the seeking of new data and the willingness to rigorously test hypotheses continue to be essential in further elucidation of the functions of TRP channels. □

1. Sukharev, S. & Corey, D. P. *Science's STKE* **219,** re4 (2004).
2. Corey, D. P. *et al. Nature* doi 10.1038/nature03066 (2004).
3. Maroto, R. *et al. Nature Cell Biol.* **7,** 179–185 (2005).
4. Clapham, D. E. *Nature* **426,** 517–524 (2003).
5. Nilius, B. *Science's STKE* **243,** pe36 (2004).
6. Story, G. M. *et al. Cell* **112,** 819–829 (2003).
7. Jordt, S.-E. *et al. Nature* **427,** 260–265 (2004).
8. Christensen, O. *Nature* **330,** 66–68 (1987).
9. Wes, P. D. *et al. Proc. Natl Acad. Sci. USA* **92,** 9652–9656 (1995).
10. Hamill, O. P. & Martinac, B. *Physiol. Revs* **81,** 685–740 (2001).
11. Voets, T. *et al. Nature* **430,** 748–754 (2004).
12. Rosado, J. A. & Sage, S. O. *Biochem. J.* **356,** 191–198 (2001).
13. Vaca, L. & Sampieri, A. *J. Biol. Chem.* **277,** 42178–42187 (2002).
14. Mori, T. *et al. J. Exp. Med.* **195,** 673–681 (2002).
15. Chen, J. & Barritt, G.J. *Biochem. J.* **373,** 327–336 (2003).

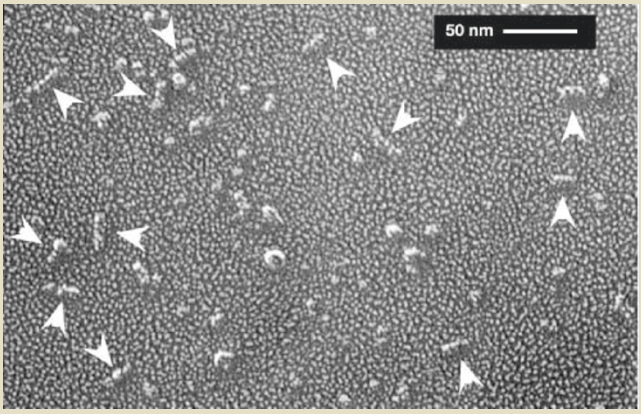
Spire: a new nucleator for actin

Dyche Mullins and colleagues have revealed a new way to kick-start actin polymerization. Reporting in the 27 January issue of *Nature* (Quinlan *et al.* doi: 10.1038/nature03241), they show that Spire, known to regulate polarity of both oocytes and embryos during *Drosophila* development, represents a third class of actin nucleator that seems to work in its own unique way.

Previous to this study, we have only been aware of two factors capable of nucleating actin polymerization *in vivo*: the Arp2/3 complex and the formin family of proteins. Spire, which shows no sequence homology to these factors, first attracted the attention of Mullins and colleagues because it contains actin-binding domains found in regulators of the Arp2/3 complex such as N-WASP. So it was a surprise to find that, unlike these Arp2/3 regulators, Spire can trigger actin nucleation on its own.

Spire seems to tackle actin polymerization by an unprecedented mechanism, sharing only limited functional hallmarks with the Arp2/3 complex and formins. It acts independently of the Arp2/3 complex to trigger actin assembly *in vivo* and induce formation of new filaments *in vitro*. Its efficiency is similar to that of formins and, unlike the Arp2/3 complex, Spire does not seem to bind to the sides of existing filaments and does not generate a branched actin network. Similarly to the Arp2/3 complex, however, Spire remains bound to the pointed end of newly formed actin filaments.

Mullins and colleagues also pinpointed the regions of Spire that endow it with nucleation activity: these include its four WASP homology 2 (WH2) domains and a unique actin-binding site found in one of the linker domains. This is particularly intriguing because tandem WH2 domains found in other actin regulatory proteins such as N-WASP are not able to nucleate actin polymerization. The two most C-terminal WH2 domains in Spire seem to be most critical and, from their biochemical data, the authors predicted that Spire binds up to four actin monomers and assembles them into a tetramer capable of nucleating filament formation. They were able to confirm this through electron microscopy studies of Spire bound to actin in conditions that would capture events before filament elongation.



Spire, a novel nucleator of actin polymerization, binds to actin and forms a rod-shaped structure consistent with four actin monomers aligned along their long axes. Figure reproduced with permission from *Nature* doi:10.1038/nature03241 © (2005) Macmillan Magazines Ltd.

Thus, Spire completes a trio of factors able to nucleate new actin filaments. It is clear that each of these comes into its own in particular biological contexts requiring distinct filament architectures. But given the diverse biological repertoire of actin dynamics, how many more nucleators remain to be discovered, and how many ways have they evolved to manipulate actin?

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