convergent extension. According to the authors, a different signalling molecule, Nodal, rather than activin, is likely to be responsible for controlling A–P patterning *in vivo*.

In a final set of experiments, the impairment of the Wnt/planar cell polarity (PCP) pathway prevented the elongation of explants, but did not disturb the graded gene-expression pattern. So, Wnt/PCP signalling seems to control convergent extension independently of A–P polarity, which indicates that the two pathways probably function in parallel.

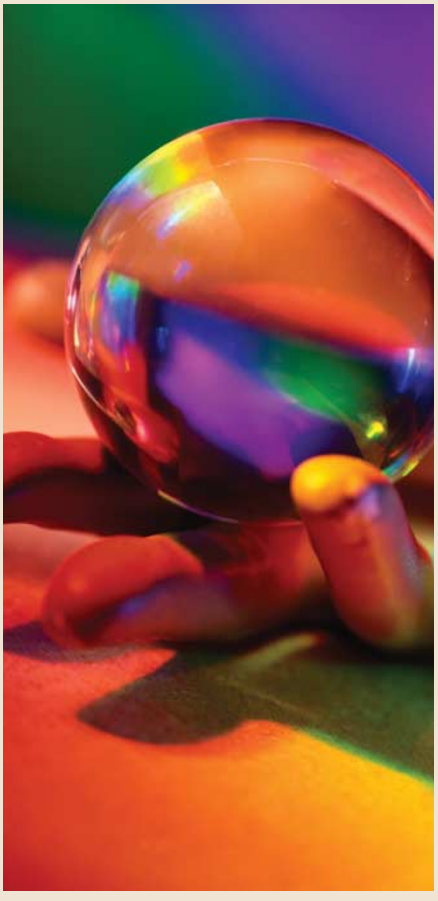
Together, these new findings pave the way for investigating the specific cellular properties that make polarized chordamesoderm cells intercalate, and converge and extend along the A–P axis, thereby separating head from tail.

Arianne Heinrichs

References and links

ORIGINAL RESEARCH PAPER Ninomiya, H. *et al.* Antero–posterior tissue polarity links mesoderm convergent extension to axial patterning. *Nature* **430**, 364–367 (2004)

FURTHER READING Keller, R. Heading away from the rump. *Nature* **430**, 305–306 (2004)



PROTEIN DEGRADATION

Be more choosy

The selection of substrates for degradation by the 26S proteasome is generally thought to lie at the level of ubiquitin-chain assembly. But, in *Cell*, Verma, Deshaies and colleagues now show that the proteins that link polyubiquitylated substrates to the proteasome can add a further layer of substrate selectivity.

The recruitment of polyubiquitylated substrates to the proteasome is essential for ubiquitin-selective degradation, but which protein recognizes the polyubiquitin chains? So far, three different proteins — Rpn10, Rad23 and Rpt5 — have been proposed to be involved in this recognition, and Verma, Deshaies and co-workers addressed the issue of substrate recruitment by studying the degradation of a polyubiquitylated yeast protein (UbSic1) *in vitro*.

They found that, whereas wild-type proteasomes degraded UbSic1 quickly, *rpn10*Δ or *rad23*Δ proteasomes were largely defective in this degradation. These defects could be rescued by the addition of an optimal amount of recombinant Rpn10 or Rad23 to either mutant proteasome, although the rescue of *rpn10*Δ proteasomes by recombinant Rad23 was weak. So, what does this mean?

Verma *et al.* found that the rescue of *rpn10*Δ proteasomes by recombinant Rad23 could be enhanced by the addition of the von Willebrand A (VWA) domain of Rpn10. This Rpn10 construct lacks its ubiquitin-interacting motif (UIM), which highlights two points.

First, the ubiquitin-binding domains of Rpn10 and Rad23 do not have to function sequentially — in fact, the authors found that Rad23 and the UIM of Rpn10 function redundantly, and in parallel, to recruit UbSic1 to proteasomes. Second, the VWA domain of Rpn10 seems to facilitate the Rad23-mediated degradation of UbSic1. Furthermore, as the VWA domain of Rpn10 was not required for the Rad23-dependent tethering of UbSic1 to the proteasome, the authors propose that it functions downstream of Rad23 to enable the productive engagement of proteasome-bound substrates by the degradation machinery.

Next, the authors confirmed their results *in vivo*. Consistent with their proposal that Sic1 can be targeted for degradation by Rad23 or the UIM of Rpn10, they showed that Sic1 was significantly stabilized in cells that were mutated for both Rad23 and the UIM of Rpn10 (Sic1 was degraded with normal kinetics in *rad23*Δ cells). Furthermore, consistent with the proposed facilitator function of Rpn10, Sic1 was more stable in *rpn10*Δ cells than in cells that were only mutated for the UIM of Rpn10 — that is, in the presence of Rad23, Sic1 is more stable in the absence of the VWA domain of Rpn10.

In the final part of this study, Verma, Deshaies and co-workers studied the degradation of other proteasome substrates and found that there was an unexpected degree of specificity in the requirement of substrates for different polyubiquitin-binding proteins. On the basis of their results, they propose that Rpn10, Rad23 and Dsk2 (a protein that is similar to Rad23), and possibly Rpt5 and Ufd1–Cdc48 (a complex that is involved in endoplasmic-reticulum-associated degradation) can function separately to recruit polyubiquitylated substrates to the proteasome. The challenges for the future are to elucidate how many recruitment pathways exist, to understand how substrates are targeted to the different pathways, and to determine whether the different pathways are differentially regulated.

Rachel Smallridge

References and links

ORIGINAL RESEARCH PAPER Verma, R. *et al.* Multiubiquitin chain receptors define a layer of substrate selectivity in the ubiquitin–proteasome system. *Cell* **118**, 99–110 (2004)

FURTHER READING Pickart, C. M. & Cohen, R. E. Proteasomes and their kin: proteases in the machine age. *Nature Rev. Mol. Cell. Biol.* **5**, 177–187 (2004)

WEB SITE

Ray Deshaies' laboratory: http://www.its.caltech.edu/~rjdlab/