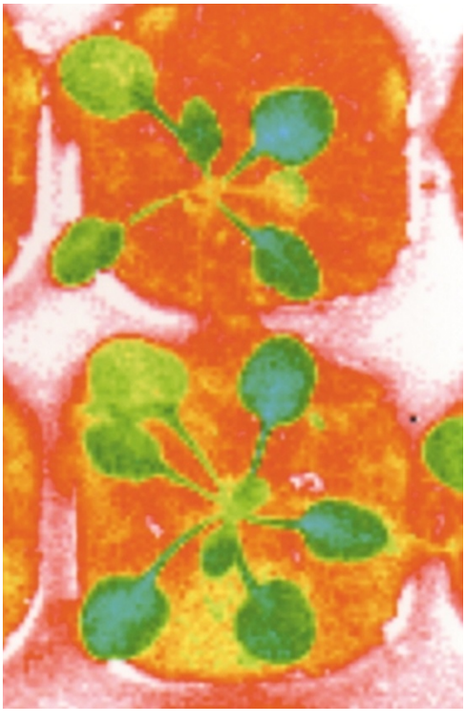

matrix could increase its permeability, thereby enlarging the suppressor's area of influence.

Whatever the role of HIC, showing its involvement in CO_2-induced changes in stomatal density is the first step in revealing how plants adjust their development to cope with global environmental change.

Christopher Surridge
Senior Editor, Nature

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WEB SITE The *Arabidopsis* Information Resource

parkin mutants didn't.

Does parkin have other substrates, and is one of CDCrel-1's normal functions to block dopamine release? If it is, blockage of CDCrel-1's breakdown in ARJP would provide a satisfactory explanation and a promising therapeutic target for this form of Parkinson's.

Cath Brooksbank

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MEIOSIS

Synapsis spoilt

Synapsis — the process by which paired homologous chromosomes are brought into close alignment — is a general feature of meiosis. But whereas *S. cerevisiae* requires a protein called Spo11p to initiate synapsis, *C. elegans* and *Drosophila* do not. Because Spo11p and its homologues generate double-stranded DNA breaks (DSBs) — which initiate meiotic recombination — one model for synapsis is that, in worms and flies at least, it occurs in specialized 'pairing centres', without the need for meiotic recombination.

Could a dependence on pairing centres have emerged with increased genome complexity? And, if so, might mammals rely on such centres? Two papers in *Molecular Cell* report that, surprisingly, they don't.

Both groups have knocked out the mouse *Spo11* gene, and they find that both male and female mice have severe gonadal abnormalities from defective meiosis. Moreover, two 'markers' for meiotic recombination — Rad51 and Dmc1, which load onto single-stranded DNA ends at the sites of DSBs — do not form characteristic foci in the *Spo11*$^{-/-}$ mice. In other words, synapsis in mice seems to depend on meiotic recombination.

Romanienko and Camerini-Otero also propose a second function for Spo11 in mice. They localized the Spo11 protein in meiotic chromosome spreads, and saw that it decorated the lengths of synapsed homologues during pachytene. This was unexpected — Spo11 is thought to catalyse the formation of DSBs at an earlier stage, leptotene. But, because pachytene is the stage at which homologous pairs become fully synapsed, the authors suggest that Spo11 could also have a structural function in stabilizing synapsis.

Alison Mitchell

References and links

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PROTEIN–PROTEIN INTERACTIONS

Phosphothreonine lego

Protein phosphorylation can work in two ways: like lego, allowing other proteins to snap into place; or like a switch, triggering a conformational change. Not long ago, dogma decreed that phosphotyrosine was a lego builder whereas phosphoserine and phosphothreonine were conformational switchers. A paper by Daniel Durocher and colleagues in *Molecular Cell* provides definitive evidence that serine/threonine phosphorylation can build lego too.

In 1999 the same team discovered that the forkhead-associated (FHA) domain — first identified in forkhead transcription factors but now known to be present in many other proteins — is a phosphopeptide recognition motif. They have now used a peptide library to find the optimal binding sequences for several FHA domains, including the two (FHA1 and FHA2) in yeast Rad53p, which binds phosphorylated Rad9p in response to DNA damage. They found that, just like the phosphotyrosine-binding SH2 domain, FHA domains recognize phosphothreonine in the context of flanking amino acids, so individual FHA domains bind specifically to different peptides. Peptide binding depends absolutely on phosphothreonine (its replacement with phosphoserine blocks binding), but the surrounding residues generate specificity. For example, Rad53p's FHA1 domain strongly prefers aspartate three residues downstream of the phosphothreonine (the +3 position), whereas the FHA2 domain prefers isoleucine. Other residues between the –3 and +3 positions also influence binding affinity but, although there are some exceptions, in general the strongest selection depends on an FHA domain's preference at the +3 position.

The crystal structure of Rad53p's FHA1 domain bound to a longer peptide containing its optimal binding sequence revealed why the +3 residue is so important (see picture). Phosphothreonine and Arg+3 make the largest number of direct contacts with the FHA domain. Another intriguing observation is that the FHA domain's fold is identical to that of the MH2 domain in SMAD transcription factors — proof that you can teach an old fold new tricks. But perhaps the most exciting prospect is that this work allows us to trawl the sequence databases for specific FHA-domain-binding proteins. This should help us to build better models of DNA-damage response pathways and other processes that involve proteins containing FHA domains.

Cath Brooksbank

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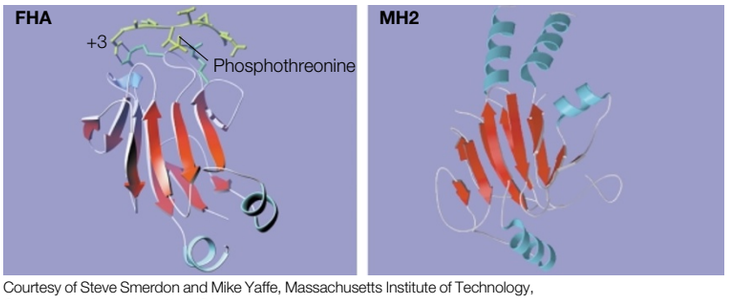

Courtesy of Steve Smerdon and Mike Yaffe, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA.