RESEARCH HIGHLIGHTS

Plant RNAi: not so lost for translation

Plant non-coding microRNAs (miRNA) were thought to induce mRNA cleavage, in contrast to animals where a low level of complementarity with the target excludes the cleavage machinery and inhibits translation instead. By looking for mutants that no longer silence a GFP reporter carrying an endogenous miRNA-binding site, Voinnet and colleagues (*Science* **320,** 1185–1190; 2008) show that miRNAs can also trigger translation inhibition in *Arabidopsis*. Analyses of known endogenous miRNA–mRNA target pairs show that this phenomenon is widespread and does not depend on a low degree of complementarity or on the position of the miRNA target sequence within the mRNA. One of the regulators identified is the microtubule-severing enzyme Katanin, thereby highlighting a link between the cytoskeleton and miRNA-mediated silencing. The authors also showed that Argonaute 1, an effector of miRNA-induced mRNA cleavage, is essential for translation inhibition. In a final twist, they demonstrate that a short interfering (si) RNA also inhibits translation of its target, suggesting that in animals, siRNA-mediated silencing could also occur through translational control. NLB

HP1-β phosphorylation in DNA repair

Recruitment of the phosphorylated variant histone γ-H2AX is an early marker for DNA damage; however, the signals that trigger γ-H2AX phosphorylation have remained unclear. Venkitaraman and colleagues (*Nature* **453,** 682–686; 2008) have found that the dynamics of histone binding protein 1 (HP1)-β are perturbed by DNA damage. Surprisingly, there was no concomitant alteration in methylation or acetylation of histones. A consensus sequence for casein kinase 2 (CK2) phosphorylation was identified around Thr 51 of HP1-β, which is intimately involved in its interaction with chromatin. Phosphorylation of Thr 51 by CK2 was observed to increase after DNA damage, correlating with increased localization at γ-H2AX-marked sites of damage. Interestingly, fusion of HP1-β to a histone — leading to its immobilization on chromatin — blocked γ-H2AX phosphorylation in response to agents that cause DNA damage. These data suggest that mobilization of HP1-β from chromatin, triggered by CK2-mediated phosphorylation, facilitates γ-H2AX phosphorylation and subsequent repair of DNA damage. These findings highlight a mechanism for chromatin reorganization that relies not on modifying histones but rather on modification of histone-binding proteins themselves. AJ

DAP5 translates as survival in mitosis

In response to cellular stresses, the eIF4G family member DAP5 regulates IRES-driven translation of apoptosis-related transcripts when cap-dependent translation is inhibited. Adi Kimchi and colleagues (*Mol. Cell* **30,** 447–459; 2008) now report that DAP5 is also essential for the IRES-dependent synthesis of two pro-survival proteins in non-stressed cells. *DAP5* knockdown reduced cell viability through caspase-dependent apoptosis, specifically during M phase. Whereas cap-dependent translation and the global polysome profile were not affected, IRES-driven translation of the anti-apoptotic factor Bcl-2 was selectively abrogated. In addition, an IRES element was identified in the 5′UTR of the mitotic kinase CDK1, and CDK1 translation was also impaired in DAP5-deficient cells during mitosis. This caused a decrease in phosphorylation of CDK1 target proteins, indicating that *de novo* synthesis of CDK1 is crucial for its cellular functions and cell survival during mitosis. Ectopic expression of Bcl-2 or CDK1 partially prevented mitotic cell death triggered by *DAP5* knockdown. Together with previous work in mouse, zebrafish and *Drosophila melanogaster* showing that DAP5 is essential during development, these findings suggest that other unknown DAP5 targets may have equally crucial cellular functions. SG

Short-circuiting the damage checkpoint

Many components of the DNA damage sensing system that leads to cell-cycle checkpoint activation are known. David Toczyski and colleagues (*Mol. Cell* **30,** 267–276; 2008) now show that colocalization of a subset of the sensors on DNA is sufficient to activate the checkpoint independently of damage in *Saccharomyces cerevisiae*. The damage response requires the kinases ATM and ATR (Tel1 and Mec1 in *S. cerevisiae*). Mec1 binds to processed double-stranded breaks through Ddc2, leading to phosphorylation of Rad9 (mammalian 53BP1), which activates the kinase Rad53 (mammalian Chk2). On the other hand, the checkpoint response also requires independent localization of the 9-1-1 complex (Ddc1/hRad9, Mec3/hHus1, Rad17/hRad1) to damaged DNA. Toczyski and colleagues found that expression of chimaeric proteins containing LacI fused to Ddc2 and Ddc1 or Mec3 trigger checkpoint activation in strains harbouring arrays of LacI-binding sites. Interestingly, of the 9-1-1 complex only Ddc1 was required to activate Mec1 and the checkpoint. Activation of the checkpoint was proportional to the number of damage sensors tethered to DNA and required the appropriate chromatin context, but no DNA damage. The authors used this elegant tethering approach to verify that CDK phosphorylation of Rad9 has a role in checkpoint activation and undoubtedly will pursue a systematic dissection of the DNA damage response. BP

Capping protein negotiates actin nucleation

An apparent paradox — that capping protein (CP), terminates elongation of actin filaments while also increasing actin network assembly and cell motility — has been resolved by Dyche Mullins and colleagues (*Cell* **133,** 841–851; 2008) with the finding that CP promotes Arp2/3-mediated filament nucleation. In several cellular contexts, including the leading edge of migrating cells, the Arp2/3 actin-nucleation complex promotes the assembly of new filaments from the sides of existing ones, producing a branched actin network. Previously, CP was proposed to increase actin network assembly by 'funnelling' actin monomers towards elongating filaments. Using purified components to reconstitute actin-based motility of beads *in vitro*, Mullins and colleagues found that the main effect of CP is to increase the rate of Arp2/3-dependent filament formation. They suggest a new model, in which CP shunts actin monomers away from capped barbed ends towards sites of Arp2/3 to promote nucleation. Rather than changing the number of free barbed ends or the overall rate of actin polymerization, the main function of CP is to change the architecture of the actin network — with important consequences for the rate of motility. AS

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