RESEARCH HIGHLIGHTS

A deubiquitylase for Polycomb repressive complex proteins

The Polycomb repressive complex 1 (PRC1) represses transcription by catalyzing mono-ubiquitylation of histone H2A. In *Nature*, Müller and colleagues identified a deubiquitylase (PR-DUB) associated with PRC1 that deubiquitylates H2A and relieves gene repression (*Nature* 465, 243–247; 2010). Peters and colleagues now show that the deubiquitylases USP7 and USP11 also form part of the PRC1 complex and modulate transcription of the *INK4a* tumour-suppressor locus by regulating ubiquitylation of PRC1 complex proteins rather than histones (*EMBO J.* doi:10.1038/emboj.2010.129) .

USP7 and USP11 were identified as novel PRC1 complex components that interact with chromatin. The PRC1 components MEL18 and BMI1 repress transcription of *INK4a*. Intriguingly, despite the ability of USP7 to deubiquitylate H2A *in vitro*, shRNA-mediated reduction of USP7 and USP11 de-repressed *INK4a* transcription and induced cellular senescence. Moreover, knockdown or overexpression of USP7 or USP11 did not affect H2A ubiquitylation *in vivo*. Depletion of these deubiquitylases instead caused a marked reduction in MEL18 and BMI1 protein levels, whereas their overexpression reduced ubiquitylation of MEL18 and BMI1. Thus, these deubiquitylases modulate transcriptional repression of *INK4a* by regulating the levels of PRC1 complex components, revealing an additional mechanism by which PRC-associated deubiquitylases can affect gene transcription. EJC

Dissecting the spindle assembly checkpoint

The spindle assembly checkpoint (SAC) restrains chromosome separation by inhibiting the APC/C activator Cdc20 until all kinetochores are attached to the microtubules. Among the SAC components is the kinase Mps1, although its precise role is unclear. Mps1 is also needed for chromosome bi-orientation and is suggested to regulate Aurora B.

Now three groups have expanded the known roles for Mps1, as reported in the July issue of *The Journal of Cell Biology*, using different techniques to inactivate the kinase. Jallepalli and colleagues (*J. Cell Biol.* **190,** 89–100; 2010) replaced endogenous Mps1 with a version sensitive to bulky purine analogues. Interphase inhibition of Mps1 releases Mad2 and BubR1 from Cdc20, demonstrating that Mps1 is needed for a previously suggested timing mechanism that prevents premature anaphase onset. Accordingly, mitosis is accelerated in the absence of Mps1 activity. Interestingly, Mps1 can assemble inhibitory Cdc20 complexes without being localized to kinetochores. They also show that inhibition of Mps1 in mitosis prevents SAC components from accumulating at the kinetochore. This is supported by Mussachio and colleagues (*J. Cell Biol*. **190,** 73–87; 2010) who find that Reversine, a drug described as an Aurora inhibitor, is actually more effective against the Mps1 kinase. This group also shows that Aurora B activity is required for Mps1 phosphorylation and for its kinetochore localization, suggesting that Auora B is upstream, rather than downstream of Mps1. They find that Mps1 is required for the correction of erroneous microtubule–kinetochore attachments. Finally, Taylor and colleagues, (*J. Cell Biol*. **190,** 25–34; 2010) find a new Mps1 inhibitor in a compound screen. They demonstrate a specific requirement for Mps1 in the continuous recruitment of O-Mad2 to a stable Mad1–C-Mad2 kinetochore core complex in mitosis.

All three groups confirm a role for Mps1 in chromosome bi-orientation, but suggest this is independent of Aurora B. Rather, Jallepalli and colleagues propose that Mps1 functions through recruitment of Bub1 and its effectors BubR1 and Shugoshin to the outer kinetochore and inner centromere, respectively. Further work is needed to pin down exactly how Mps1 exerts these roles and what its substrate(s) are. CKR

Staying within boundaries

The conserved protein complex PAR-6–aPKC–PAR-3 (PAR complex hereafter) localizes to the anterior cortex of one-cell *Caenorhabditis elegans* embryos. LGL is found at the basolateral region of epithelial cells where it modulates polarity. Using a biochemical approach to search for PAR-6 interacting proteins in *C .elegans*, Hyman and colleagues identify LGL and show that in one-cell embryos the anterior PAR complex and posterior LGL function through 'mutual elimination' to maintain opposing cortical domains that regulate partitioning of cell fate determinants (*Curr. Biol*. doi:10.1016/j.cub.2010.05.061).

Despite its interaction with the anterior complex, LGL is localized to the posterior cortex, as is the polarity protein, PAR-2. LGL requires both PAR-2 and an intact PAR complex for this localization. Although *lgl* mutants do not exhibit a polarity phenotype, they are hypersensitive to loss of *par-2*, and GFP–LGL rescues *par-2* mutant phenotypes, including the correct partitioning of cortical PAR complex and of cytoplasmic determinants. Further biochemical and functional analysis reveals that PKC-3-dependent phosphorylation of LGL is required for LGL polarizing activity and restriction to the posterior. The authors propose a model whereby LGL binds to the PAR complex at the anterior–posterior boundary and is then phosphorylated by PKC-3, inducing release of the PAR-6–aPKC–PAR-3–LGL complex from the cortex and preventing spreading of the PAR complex to the posterior LGL domain. It remains to be seen if LGL phosphorylation functions similarly to regulate cortical domain boundaries in other systems. NLB

A coat for ciliary trafficking

Primary cilia project from nearly every cell in vertebrates and function as antennae, containing receptors that pick up signals involved in pathways such as phototransduction and olfaction. However, how the receptors get to the membranes of the cilia has been a mystery. Now, Nachury and colleagues (*Cell* **141,** 1208–1219; 2010) have found that proteins involved in Bardet-Biedl syndrome (BBS) have a role in localizing receptors to cilia membranes.

The authors found that Arl6, a BBS protein, binds to the BBSome (a complex made up of seven BBS proteins and a novel protein, BBIP10). Immunostaining and super-resolution imaging showed that BBSome components and Arl6 co-localize to the primary cilia. Arl6, an Arf-like GTPase, is related to a family of proteins involved in recruiting coat complexes — proteins that construct vesicles, and help recognise and sort the molecules that the vesicles carry — to membranes. Consistent with this, the BBSome forms a coat around liposomes *in vitro*, which is mediated by Arl6. Furthermore, the authors demonstrate that the BBSome can recognise and transport a receptor protein to cilia.

The authors suggest that the variety of symptoms associated with BBS may result from a failure to transport signalling receptors to primary cilia. GD

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