that a lack of RB1 didn't alter the expression levels of Suv4-20h. By overexpressing fluorescently tagged HMTases they confirmed that these enzymes were properly recruited to constitutive heterochromatin in TKO cells. These overexpressed HMTases could rescue the decreased H4K20 tri-methylation, so the authors concluded that this phenotype was the result of decreased Suv4-20h activity, indicating that RB1 proteins stabilize H4K20 tri-methylation by these HMTases. Finally, the authors showed direct binding of RB1, RBL1 and RBL2 to Suv4-20h1 and Suv4-20h2 *in vitro*, but not *in vivo*.

Altogether, this new study impressively shows that RB1 proteins are not only transcriptional repressors of specific target genes, but also have a role in the assembly of constitutive heterochromatin. Loss of RB1 therefore not only results in de-repression of specific promoters, but also in the global loss of a repressive chromatin state. Given this, RB1 seems to have made a quantum jump from a specific to a global tumour suppressor.

Markus Wagner,
Nature Cell Biology

References and links

ORIGINAL RESEARCH PAPER Gonzalo, S. *et al.* Role of the Rb family in stabilizing histone methylation at constitutive heterochromatin. *Nature Cell Biol.* 6 Mar 2005 (doi:10.1038/ncb1235)

FURTHER READING Liu, H. *et al.* New roles for the RB tumor suppressor protein. *Curr. Opin. Genet. Dev.* **14**, 55–64 (2004)

WEB SITE

María Blasco's laboratory: http://www.cnio.es/ing/programas/prog102.asp

much sooner at the Golgi. Total inhibition of palmitoylation blocked trafficking from the PM to the Golgi and therefore blocked Ras activation.

So, rapid exchange of palmitoylated Ras isoforms at the PM and Golgi is driven by de- and re-palmitoylation cycles. De-palmitoylation confers an equal distribution between the cytosol and membranes. Re-palmitoylation, which enables stable membrane anchorage, occurs at the Golgi; from here, Ras is redirected to the PM in the exocytic pathway. As the authors' findings of such a cycle extended to other proteins that have been reported to localize to the PM and the Golgi, they propose that this process has a universal role in subcellular distribution.

Katrin Bussell

References and links

ORIGINAL RESEARCH PAPER Rocks, O. *et al.* An acylation cycle regulates localization and activity of palmitoylated Ras isoforms. *Science* 11 Feb 2005 (doi:10.1126/science.1105654)

FURTHER READING Hancock, J. F. Ras proteins: different signals from different locations. *Nature Rev. Mol. Cell Biol.* **4**, 373–385 (2003)

IN BRIEF

DNA REPAIR

Conserved modes of recruitment of ATM, ATR and DNA-PKcs to sites of DNA damage.

Falck, J. *et al. Nature* 2 Mar 2005 (doi:10.1038/nature03442)

The phosphoinositide-3-kinase-related protein kinase (PIKK)-family members ATM, ATR and DNA-PKcs are activated in response to DNA damage and recruited to sites of DNA damage by individual partner proteins. Falck *et al.* have now identified a conserved interaction motif in the C terminus of each partner protein — Nbs1, ATRIP and Ku80, respectively — that is essential for the recruitment of these PIKKs as well as for the downstream signalling events.

CHROMOSOME SEGREGATION

Dissociation of cohesin from chromosome arms and loss of arm cohesion during early mitosis depends on phosphorylation of SA2.

Hauf, S. *et al. PLoS Biol.* **3**, e69 (2005)

Shugoshin prevents dissociation of cohesin from centromeres during mitosis in vertebrate cells.

McGuinness, B. E. *et al. PLoS Biol.* **3**, e86 (2005)

During mitosis, sister chromatids are held together by cohesin, which is cleaved in anaphase, triggering chromatid segregation. However, most cohesin is removed from the chromosome arms, but not from the centromere, before anaphase. One study now shows that phosphorylation of the cohesin subunit SA2 is required for cohesin removal from chromosome arms in early mitosis. So what safeguards centromeric cohesin? Shugoshin, according to a second study, as this protein seems to protect centromeric SA2 from phosphorylation to prevent premature chromatid segregation.

PLANT BIOLOGY

RNA polymerase IV directs silencing of endogenous DNA.

Herr, A. J. *et al. Science* 3 Feb 2005 (doi:10.1126/science.1106910)

Plant nuclear RNA polymerase IV mediates siRNA and DNA methylation-dependent heterochromatin formation.

Onodera, Y. *et al. Cell* 10 Feb 2005 (doi:10.1016/S0092867405001510)

Plants encode catalytic subunits of a fourth RNA polymerase, Pol IV, the function of which has remained unknown, until now. Data from two studies now indicate that Pol IV causes small interfering (si)RNA-mediated gene silencing and facultative heterochromatin formation. These events are associated with RNA-directed DNA methylation, which requires siRNAs for targeting specific *de novo* DNA-methylation events. The production of siRNAs might be mediated by a mechanism that involves Pol IV, although its precise role is yet to be determined.