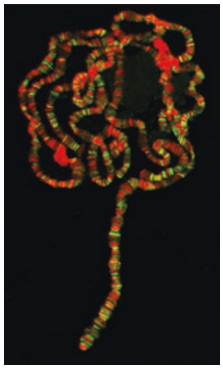
A double agent



Post-translational histone modifications, such as acetylation, methylation, phosphorylation and ubiquitination, mark the transcriptional state of the chromatin. These markings, and the resulting gene expression patterns, can be inherited through cell division. Recent research has significantly advanced our understanding of the effects of histone acetylation and methylation on gene expression, but the roles of histone ubiquitination in transcription regulation are only beginning to emerge. Verrijzer and colleagues have now examined whether a ubiquitin-specific protease, Usp7, plays a role in the regulation of gene expression in *Drosophila*. They showed that Usp7 is associated with the polytene chromosome at specific, silenced loci, including those that contain genes repressed by the Polycomb (Pc) protein. Genetic experiments show that *Usp7* enhances the repressor activity of Pc. Surprisingly, the Usp7 protein is tightly associated with a metabolic enzyme, guanosine 5′ monophosphate synthase (GMPS), and the Usp7–GMPS complex specifically removes the ubiquitin moiety from modified H2B. The deubiquitinase activity of Usp7 toward H2B requires the GMPS interaction, but the catalytic activity of GMPS is dispensable. Thus, GMPS does double duty in the cell: biosynthesis of GMP and activation of a nuclear deubiquitinating enzyme. The authors speculate that the regulation of Usp7 by GMPS, an enzyme in the guanine nucleotide biosynthesis pathway, may link the metabolic state of a cell with the gene silencing activity of Pc, and this link may be important for maintaining the tight coupling between cell division, cell growth and differentiation during development. (*Mol. Cell* **17**, 695–707, 2005) *HPF*

ROCK and RhoE

The Rho family of GTPases are involved in the regulation of cytoskeleton dynamics. They cycle between an active, GTP-bound form and an inactive, GDP-bound form. The Rnd proteins, of which RhoE is a member, form a separate and distinct branch in the Rho family. RhoE has very low intrinsic GTPase activity and exists mostly in a GTP-bound state. This prompts the question of whether RhoE is regulated by a mechanism unrelated to GTP hydrolysis. Previous studies had shown that RhoE expression is stimulated by platelet-derived growth factor (PDGF) and that RhoE binds to and inhibits the serine/threonine kinase ROCK I. Increases in RhoE levels were also shown to correlate with changes in cell morphology, for example, the loss of actin stress fibers. Ridley and colleagues now show that RhoE is phosphorylated. This phosphorylation increases RhoE stability in the cell and correlates with RhoE-mediated disruption of stress fiber formation. In addition, they show that PDGF receptor activation stimulates RhoE phosphorylation via a protein kinase C pathway, and that RhoE is a ROCK I target and may also be a target for other kinases. These results implicate RhoE in a negative feedback loop for ROCK I, where ROCK I-mediated phosphorylation stabilizes RhoE and allows it to inhibit ROCK I. They also show that phosphorylation may control RhoE's role in actin filament disruption. (*EMBO J.* advance online publication 3 March 2005, doi:10.1038/sj.emboj.7600612) *MM*

Research Highlights written by Mirella Bucci, Hwa-ping Feng, Evelyn Jabri and Michelle Montoya

Processing bodies

Regulated mRNA decay, which is critical for post-transcriptional gene expression, begins with the shortening of the mRNA 3′ polyadenosine tail which subsequently leads to the removal of the cap structure at the 5′ end of the mRNA. This decapping process allows an exonuclease to degrade mRNA. In yeast and mammals the decapping enzyme, activators of decapping, and a 5′→3′ exonuclease are localized to discrete cytoplasmic foci called processing bodies (P-bodies) or Dcp bodies. Multiple laboratories have suggested that P-bodies are pools of mRNA that have undergone translation and are on their way to being degraded. Parker and colleagues examine the role of RNA in formation of the P-bodies, the relationship of these foci to the translating pool of mRNA, and the variation in size of these processing centers in response to stress. The data show that RNA, most likely nontranslating mRNA, is required for the assembly of P-bodies. RNase treatment of partially purified P-bodies shows that RNA is also required for the integrity of these complexes. The authors also show that the certain types of stress including glucose deprivation, osmotic stress, UV light and late stage of growth, all of which lead to inhibition of translation initiation, result in an increase in the concentration of P-bodies. The authors suggest that this increase is due to mRNAs moving from the translating ribosomes to the foci. Whether mRNAs are specifically targeted to the P-bodies or if individual mRNA-containing ribonucleoproteins come together to form a larger complex is not clear. Regardless, the mRNAs must lose their translation factors and acquire mRNA decapping proteins as they physically move between the regions of the cell containing polysomes and P-bodies. The mechanism by which the mRNA makes these transitions and how they are regulated requires further study. (*RNA* **11**, 371–382, 2005) *EJ*

Bridging the switch

The formation of specific IgG molecules within antigen-activated B cells requires rearrangement of the heavy chain locus, in a process called class switch recombination. Recombination joins a new constant region (C) to the expressed variable region, rejoining chromosomal DNA and generating a circle containing excised sequences. Switch recombination involves G-rich and repetitive sequences called 'switch' (S) regions. Switch recombination begins with transcription of the S regions and the formation of distinct G-loops. It depends on the B cell-specific cytidine deaminase, AID, as well as ubiquitous DNA repair factors. One key repair factor in switch recombination is the mismatch repair heterodimer, MutSα (MSH2–MSH6). Larson and colleagues have now developed a model for the mechanism of MutSα function. They show that in primary B cells switching to IgG3, MSH2 associates with transcribed Sγ3 regions, one of the S regions downstream of the variable region. More specifically, recombinant MutSα binds to U•G mismatches, formed by AID-initiated deamination of C-G base pairs, and to G4 DNA, a four-stranded structure spontaneously formed by G-rich sequences within the S regions. Electron microscopy data show that MutSα bound to G-loop sequences can form interactions between G-loops in separate molecules. This bridging of G-loops forms the basis of the model where MutSα promotes synapsis of transcriptionally-activated S regions and provides insight into how distant chromosomal regions may be brought together for switch recombination. (*Curr. Biol.* **15**, 470–474, 2005) *MB*