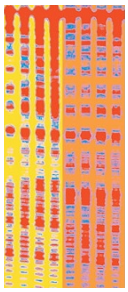
Various variants



The nucleosome blocks the accessibility of DNA to transcription factors and passage of the transcription complex machinery. The cell has a few ways to overcome this barrier, including post-translational histone modification, chromatin remodeling, and the incorporation of histone variants into the histone octamer. Histone variants are non-allelic variants of conventional histones that are present at relatively low concentrations in the cell. The insertion of variants into the histone octamer can affect chromatin properties such as assembly and stability, as well as gene regulation. H2ABbd is a recently identified variant that is considerably shorter than other H2A proteins and lacks the conserved H2A residues used in regulatory post-translational modification. In an effort to understand how it affects chromatin, Angleov *et al.* have examined the properties of H2ABbd-containing nucleosomes and nucleosomal arrays. They find that the presence of H2ABbd in nucleosomes alters nucleosome structure in a way that favors access of transcription factors to their nucleosomal binding sites. In addition, H2ABbd-containing nucleosomes are resistant to remodeling by SWI/SNF and neither SWI/SNF nor the remodeling factor ACF can induce their mobilization. The H2ABbd-H2B dimer has weaker interactions with the H3-H4 tetramer than the conventional H2A-H2B dimer, and SWI/SNF can produce additional destabilizing effects on the variant nucleosomes by promoting the transfer of the H2ABbd-H2B dimer to the tetrameric H3-H4 particle. Functional assays on reconstituted chromatin show that H2ABbd stimulates p300-dependent transcriptional activation at the level of transcriptional initiation. Overall, it seems that H2ABbd is involved in gene activation. Additional studies will be needed to understand how H2ABbd is working. (*EMBO J.* **23**, 3815–3824, 2004) *MM*

Bacterial end game

Replication of eukaryotic chromosomes is complicated by the fact that the DNA polymerases used to replicate them synthesize DNA only in the 5′ to 3′ direction. As these enzymes require both a primer to initiate DNA chains and a template sequence, the 5′ ends of the lagging strand of the DNA helix are shorter than the 3′ ends of the leading strand. Enter telomerase, a reverse transcriptase (RT) that brings in its own RNA template to create tandem DNA repeats that extend the lagging strand ends. But what about linear chromosomes and plasmids found in some bacteria? Replication of linear DNA in *Streptomyces* initiates bidirectionally from an internal origin. Extension of the recessed 5′ ends requires telomeric inverted repeats and at least two proteins, Tpg and Tap. Tap, which is thought to act as a scaffold between the DNA ends and Tpg, recognizes a folded structure generated by the 3′ overhang, then appears to recruit Tpg, which primes lagging strand DNA replication. According to this model, bacterial DNA maintenance should not require a reverse transcriptase akin to the eukaryotic telomerase. But Bao and Cohen now show that Tap protein is also associated with at least two other proteins that have substantial RT activity. These proteins are DNA polymerase I (PolA) and DNA topoisomerase I (TopA), the first example of a topoisomerase protein also bearing RT activity. When the authors mapped the RT activity within TopA, they found Asp-Asp residue doublets spaced five residues apart. This motif is common to and required for the normal activity of eukaryotic telomerases. While the authors did not detect an RNA template in the RT complex of *Streptomyces*, they did note a sequence in its genome that corresponds to the terminal 13-bp sequence of the telomeric DNA required for linear DNA replication in *Streptomyces*. This current work suggests intriguing commonality among the mechanisms that accomplish replication of telomeres within multiple kingdoms. (*Proc. Natl. Acad. Sci. (USA)* **101**, 14361–14366, 2004) *MB*

Research highlights written by Mirella Bucci, Evelyn Jabri, Boyana Konforti and Michelle Montoya.

Doing double duty

The term 'metabolic enzymes' conjures up images of complex metabolic pathways and not gene regulation processes. The report by Snyder and co-workers that Arg5,6, a mitochondrial enzyme involved in arginine biosynthesis, can specifically bind DNA and regulate the expression of both nuclear and mitochondrial target genes suggests that we need to broaden our thinking. Using proteome arrays and chromatin immunoprecipitation (ChIP/chip) they identified previously unrecognized DNA binding. A protein microarray containing most yeast proteins was probed with total yeast genomic DNA. The authors identified a large number of proteins expected to bind DNA (for example, transcription factors) but many proteins were unusual in that they were not known to interact with nucleic acids. Eight proteins were tested for association with specific chromosomal and mitochondrial regions using ChIP/chip. Each candidate protein was epitope-tagged, immunoprecipitated, and the associated DNA purified and labeled. The labeled DNAs were used to probe a yeast genomic DNA array containing the intergenic regions and the entire mitochondrial genome. Three of the eight were associated with specific DNA regions *in vivo*—one of the proteins was Arg5,6. They showed that Arg5,6 can bind DNA directly *in vitro* and determined the binding site. By comparing the level of target mRNAs in wild type and *arg5,6*Δ strains they showed that Arg5,6 can affect the levels of specific mitochondrial and nuclear mRNA transcripts. By using such unbiased proteomic approaches many more multifunctional proteins may be discovered. (*Science* **306**, 482–484, 2004) *BK*

Fine-tuning gene expression

Riboswitches are control elements located in the noncoding region of mRNA that bind small metabolites such as glycine. Binding of these molecules alters the structure of the mRNA, which controls the expression of the nearby genes by affecting transcription, translation or mRNA processing. A study from the Breaker lab begins to unravel the mechanisms by which the glycine-responsive riboswitch fine-tunes gene expression. Glycine is both an essential molecule for protein synthesis and a carbon energy source for all organisms. Bacteria must regulate the breakdown of glycine when it is limiting to avoid compromising protein synthesis. Therefore, the glycine-responsive riboswitch must sense the concentration of the small molecule with high specificity as well as act as an on-switch for the expression of proteins involved in glycine metabolism. The authors show that the riboswitch consists of two metabolite-binding elements arranged in tandem. Binding of glycine to one site improves binding at the second element by ~100- to ~1,000-fold. This cooperativity, which is comparable to that exhibited between two oxygen-binding sites in hemoglobin, allows the bacteria to activate gene expression in response to a 10-fold rather than 100-fold change in glycine concentration. In effect, the tandem arrangement improves the sensing ability of the riboswitch. How the ligand-induced structural changes at one glycine-binding site are transduced to the second site is not known but may involve structural alterations within the mRNA and/or the surrounding RNA. (*Science* **306**, 275–279, 2004) *EJ*