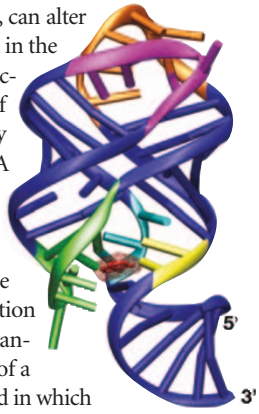
Buried in a riboswitch



Binding of small molecules, such as guanine, can alter the structure of RNA control elements found in the untranslated region of some genes. These structural alterations usually repress expression of the genes with which they are associated by affecting transcription, translation or mRNA processing. A structural and biochemical study from the Batey lab begins to unravel the nature of the conformational changes induced within one such control element, the guanine-responsive riboswitch, upon interaction with the biologically relevant substrate hypoxanthine. The structure of the complex, the first of a riboswitch, reveals a highly compact RNA fold in which the ligand sits in a pocket created by the three-way junction. While this junction is directly responsible for hypoxanthine recognition, their data show that a loop-loop interaction is also required for efficient binding. Another striking feature of the structure is that the hypoxanthine is almost completely buried within the RNA and surrounded by conserved nucleotides. Like many RNA-ligand and RNA-protein interactions, binding is accompanied by a large conformational change in the RNA. This change in the structure directs the folding of the riboswitch toward a conformation that allows the surrounding RNA to adopt a classic terminator stem-loop that stops transcription. (*Nature* **432**, 411–415, 2004) *EJ*

Pore origins

A feature of eukaryotic cells that distinguishes them from prokaryotes is the presence of membrane-bound organelles, such as the ER, Golgi and nuclear envelope. While it is generally accepted that these internal membranes originated from prokaryotic plasma membranes, it is not clear how some of the transport systems that reside in these membranes, like the nuclear pore complex (NPC), could have arisen. Recent work by the Rout and Sali labs provides a possible explanation. Using molecular modeling combined with proteolytic mapping, they propose model structures of seven nuclear pore (nup) proteins of the yeast and vertebrate NPC subcomplex yNup84/vNup107-160. The nups, which are well conserved across eukaryotes, are predicted to have a β-propeller domain, an α-solenoid domain, or a β-propeller domain followed by an α-solenoid domain. The only proteins known with this particular β-propeller/α-solenoid domain architecture are the clathrin heavy chain and homologous components of other eukaryotic coated vesicles. In addition, ySec13/vSec13R, a component of the yNup84/vNup107-160 subcomplex, is a member of a vesicle-coating complex. Therefore, the yNup84/vNup107-160 subcomplex may be related to major vesicle-coating complexes through their common architecture. Like the vesicle-coating complexes, the nups may be involved in curving membranes. Based on these observations the authors suggest that NPCs and vesicle-coating complexes may share a common ancestor or "protocoatomer" that evolved in prokaryotes to bend membranes into sheets and tubules. The ability to shape membranes would eventually lead to the formation of endomembrane systems including a primitive nuclear envelope where the NPC's progenitor could be found. (*PLoS Biol.* **2**, e380, 2004) *MM*

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

Tough breaks

Faithful DNA repair is essential for maintaining genomic stability and cell viability, and aberrant repair can lead to cell death or tumorigenesis. But before the damage can be repaired it must be recognized by the cell. Cells have developed ways to gain access to nucleosomal DNA by covalently modifying histones, promoting histone mobilization or incorporating histone variants. Modified histones can recruit chromatin-remodeling complexes to double-strand breaks. Previous studies showed that the human histone variant H2A.X and its *Drosophila* homolog, H2Av, become phosphorylated at sites of double-strand breaks. Further, double-strand breaks accumulate in the absence of the human Tip60 complex, a candidate chromatin-remodeling complex, suggesting that it may play a role in DNA repair. Workman and co-workers now demonstrate that the *Drosophila* dTip60 complex catalyzes the exchange of phospho-H2Av with unmodified H2Av. They show that the acetylation reaction is catalyzed by the histone acetyltransferase dTip60 and the exchange reaction depends on the ATPase Domino. These findings reveal a novel mechanism for histone exchange that involves the concerted action of two distinct chromatin-remodeling activities within the same complex. They also help explain the functional link between the phosphorylation of H2A.X at double-strand breaks and the role of Tip60 complexes in the repair of chromatin DNA. (*Science*, published online 4 November 2004, doi:10.1126/science.1103455) *BK*

Chaperoning transcription

Modulating the folded state of intracellular proteins is essential for cellular survival in a changing environment. To maintain an appropriate environment for protein folding, cells regulate the expression of universally conserved heat shock genes encoding stress-related proteins and chaperones that assist in different aspects of protein folding. A complex system controls the expression of these genes to ensure that the cell can respond to and survive even small changes in the folded state of its proteins. In *Escherichia coli*, a specific transcription initiation factor, σ^{32}, recruits RNA polymerase to the heat shock promoters. σ^{32} is regulated at multiple levels and responds to direct inputs from stresses as well as to changes in the levels of folded and unfolded proteins. For example, DnaK, a chaperone that maintains unfolded polypeptides in a folding-competent state and thereby prevents irreversible aggregation, is implicated in the regulation of σ^{32} activity and degradation. Gross and colleagues now show that GroELS, the essential chaperonin system in prokaryotes that binds non-native polypeptides and facilitates their refolding, also regulates both the stability and activity of σ^{32}. GroELS interacts directly with σ^{32} and this interaction modulates transcriptional activity of the heat shock genes. How the chaperonin and transcription factor interact and the mechanism by which binding of GroELS inhibits σ^{32} transcriptional activity are not clear. The data from Gross and colleagues suggest a new level of complexity in the regulation of the bacterial heat shock genes in which two different sensors of the state of cellular proteins are used to respond to small changes in global protein folding. (*Genes Dev.* **18**, 2812–2821, 2004) *EJ*