**Correlative quantum dots**

Since quantum dots were first used as fluorescent tags in a biological specimen, researchers recognized that they could potentially be used as labels for electron microscopy as well. Unfortunately, problems with loss of fluorescence and disruption of cellular structure during sample preparation have prevented their use in correlative light and electron microscopy experiments for which they seemed uniquely suited. Ellisman and colleagues have now overcome these obstacles and demonstrate that with proper specimen preparation the fluorescence of quantum dots as well as native cellular structure can be retained. Owing to the distinct emission spectra of quantum dots corresponding to different core sizes, their method allows the localization of multiple proteins in the same sample by both light and electron microscopy.

*Article p743*

**Probing nascent protein folding**

Deciphering the mechanisms by which proteins fold remains a substantial challenge for structural biology. In particular, very little is known about cotranslational folding, a process in which folding begins as the nascent protein is still emerging from the ribosome. Recognizing the dearth of methods to study this early folding event, Clark and colleagues present a strategy to stall protein translation *in vitro* or *in vivo* using a short polypeptide ‘stall sequence’ that can be inserted at virtually any point in the sequence of a recombinant protein. The conformational state of the ribosome-bound nascent protein chain can then be probed using a variety of biophysical techniques.

*Article p757*

**What’s in the apoptotic degradome?**

Programmed cell death is carried out by caspases, a specific subset of proteases; alterations in the tightly controlled activity of these enzymes have been linked to several human diseases. To gain a better understanding of caspase substrates Gevaert and colleagues present a strategy to comprehensively analyze the proteins subjected to apoptotic degradation. By comparing the pattern of cleaved N-terminal peptides in apoptotic cells to that in healthy cells using diagonal reverse-phase high-performance liquid chromatography and mass spectrometry, they identified apoptosis-specific cleavage products. Notably, they found cleavage patterns that did not conform to the canonical caspase sites, pointing to the activity of other proteases in the apoptotic cascade.

*Article p771*

**Easy esiRNAs**

Harnessing the RNA interference mechanism has allowed researchers to perform genome-wide genetic screens by systematically knocking down the expression of individual genes. *In vitro* synthesized short interfering RNAs (siRNAs) and *in vivo* expressed short hairpin RNAs are the most widely used mediators of RNA interference. However, enzymatic methods of producing large libraries of siRNAs, starting from a collection of cDNAs, have also gained popularity because they represent an economical alternative for genome-scale screens. Here Buchholz and colleagues share their protocol to make endonuclease-prepared siRNAs, or esiRNAs, using RNase III — a method which has proven versatile, efficient and cost-effective for genome-wide screens.

*Protocol p779*

**Trapping an enzyme at work**

DNA methyltransferases establish and maintain the methylation status of DNA, essential for the epigenetic regulation of gene expression. But despite the biological importance of these enzymes, scientists up to now have investigated their mechanism of action only *in vitro*. Leonhardt and colleagues now present a fluorescence-based assay to study their activity in living cells. Active DNA methyltransferases form a transient complex with DNA and are released after the transfer of a methyl group, but in the presence of a cytosine analog the active enzyme is trapped on the DNA. By measuring the fluorescence recovery after photobleaching of DNA methyltransferase-GFP fusion proteins, Leonhardt’s team can differentiate between an active enzyme, which does not allow fluorescence recovery, and an inactive enzyme, which does. This assay will allow them to screen small-molecule inhibitors that inactivate DNA methyltransferases, and it holds great promise for the development of novel enzyme inhibitors that may well be of clinical importance.

*Article p751, News and Views p736*