they call TimeSTAMP that encodes the NS3 protease flanked by two cleavage sites. Placed between the target protein and a detection tag of choice, this cassette provides two cleavage sites that could be used to remove the detection tag from the protein. When expressed in cells, the tag is constitutively removed by the protease, but application of the inhibitor retains the tag on newly synthesized protein, allowing it to be visualized. To visualize total protein, they placed a second nonremovable detection tag between TimeSTAMP and the target protein (**Fig. 1**).

They tested TimeSTAMP by tagging a major structural protein in synapses, PSD-95, that gradually accumulates in new synapses. "We wanted to know whether we could track the state of synaptic growth by looking at the rate of accumulation of PSD-95," says Lin. TimeSTAMP showed that PSD-95 was present in proportionately higher amounts in growing synapses. To demonstrate the ability of TimeSTAMP to map new protein distribution in a living animal they created transgenic *Drosophila melanogaster* expressing a TimeSTAMP-tagged protein kinase, CaMKII, whose expression in neurons is modulated by neuronal activity. The researchers observed regional and subcellular heterogeneity of new protein expression (**Fig. 1**).

The same principle behind TimeSTAMP should be adaptable to uses other than visualization of newly synthesized proteins. Replacing the detection tag with a regulatory domain should open up new applications by allowing simple temporal regulation of protein function in whole animals.

Daniel Evanko

RESEARCH PAPERS

Lin, M.Z. *et al.* A drug-controllable tag for visualizing newly synthesized proteins in cells and whole animals. *Proc. Natl. Acad. Sci. USA* **105**, 7744–7749 (2008).

one nucleosome with ubH2B and the other with its unmodified counterpart. However, efficient methylation occurred only when ubH2B was in the same nucleosome. "The ubiquitin mark may be transient and the methylation persists much longer," McGinty says, suggesting an explanation for the difference, and adds that other factors could be involved *in vivo* and a clearer picture will come from further genetics studies.

For now, he believes they developed a generalizable strategy for site-specific attachment of ubiquitin that can be used on other histones as well as nonhistone proteins. The synthetic ubH2B can be used to study the role of this modification in other methylation events as well as in transcriptional events and DNA damage repair.

To continue to decipher the histone code, McGinty suggests taking the synthetic system a step further: "You can imagine combining this strategy with other chemical tools to build engineered nucleosomes and engineered chromatin arrays with combinations of modifications at specific sites in the array, and I think it's going to be a very powerful tool in trying to dissect all of the correlative information about each of these modifications."

Irene Kaganman

RESEARCH PAPERS

Chatterjee, C. *et al.* Auxiliary-mediated site-specific peptide ubiquitylation. *Angew. Chem. Int. Ed. Engl.* 46, 2814–2818 (2007).

McGinty, R.K. *et al.* Chemically ubiquitylated histone H2B stimulates hDot1L-mediated intranucleosomal methylation. *Nature* 453, 812–816 (2008).

NEWS IN BRIEF

IMAGING AND VISUALIZATION

Nonblinking quantum dots

Single-molecule fluorophore emission intensities fluctuate between bright and dark states, a phenomenon known as blinking. This can make the interpretation of single-molecule data very difficult. Mahler *et al.* now present a method to synthesize CdSe-CdS core-shell quantum dots in which blinking is suppressed owing to a thick crystalline CdS shell. The researchers hope the nonblinking quantum dots will find application in single-particle tracking experiments.

Mahler, B. *et al. Nat. Mater.*, published online 22 June 2008.

STEM CELLS

Transcription factor binding in stem cells

Although it is clear that several transcription factors are important for maintaining pluripotency in embryonic stem cells (ESCs), the targets and downstream effectors of these transcriptional programs are far from fully understood. Chen *et al.* now use chromatin immunoprecipitation followed by sequencing, ChIP-Seq, to map the binding locations of 13 transcription factors and two co-regulators in mouse ESCs. This resource will be useful for studying the regulatory networks underlying ESC identity.

Chen, X. *et al. Cell* **133**, 1106–1117 (2008).

GENOMICS

Managing sequencing data with EagleView

Next-generation DNA sequencing technologies are facilitating rapid and low-cost sequencing of whole genomes. The enormous volume of sequencing data, however, has presented a huge data management challenge, especially in terms of data visualization. Huang and Marth now present EagleView, a data-integration and visualization tool that supports viewing of millions of reads and is capable of integrating genome annotations. The software is freely available.

Huang, W. & Marth, G. *Genome Res.*, published online 11 June 2008.

IMAGING AND VISUALIZATION

A new fluorophore for super-resolution imaging

Super-resolution imaging methods can be used to image single molecules beyond the diffraction limit in cells. Photoswitchable fluorescent proteins that have typically been used for this application are subject to photobleaching. Small organic fluorophores are more resistant to photobleaching and cause less perturbation than large fluorescent proteins but few have been developed for super-resolution imaging. Lord *et al.* now introduce a bright, photostable, photoactivatable, organic azide-based fluorophore for super-resolution imaging in living cells.

Lord, S.J. *et al. J. Am. Chem. Soc.* **130**, 9204–9205 (2008).

MICROBIOLOGY

A transposon library for *Vibrio cholerae*

Vibrio cholerae is the water-borne microorganism responsible for cholera. To facilitate genome-wide screening of gene function in this pathogen, Cameron *et al.* report the creation of a near-saturation transposon insertion library in *V. cholerae* strain C6706. They used the library to identify genes involved in chemotactic mobility, a move that may lead to new cholera vaccines.

Cameron, D.E. *et al. Proc. Natl. Acad. Sci. USA* **105**, 8736–8741 (2008).