to the original initiator. The resulting chain reaction leads to the formation of a nicked double helix that grows until the hairpin supply is exhausted. Detection of the resulting products does not require any specialized detection equipment. As Pierce remarks, "All you need is a gel apparatus, which can be found in any wet lab. We are also trying to make a nanogold-based colorimetric assay that will enable detection by eye alone."

For more diverse biosensing applications, DNA and RNA aptamers selected to bind specific molecules hold promise for the development of HCR triggers that will initiate the chain reaction only in the presence of the target molecule. The authors have used this aptamer trigger concept to specifically discriminate ATP from GTP. Pierce remarks, "If we succeed in developing a general aptamer triggering mechanism, then HCR amplification could be incorporated in sensors for a wide range of small molecules."

Unlike PCR, which provides exponential amplification, the current form of HCR provides linear amplification. "We are now developing nonlinear versions of HCR that provide quadratic, cubic or exponential growth after being triggered by the initiator," says Pierce. "However, false positives become a much bigger problem, as spurious initiation events are also amplified nonlinearly." Successful development of an exponential HCR amplification system would increase the sensitivity to target molecules at very low concentrations. This would open up the possibility of attaining a PCR-like level of sensitivity for a variety of small molecules without the need for any expensive equipment or reagents.

Daniel Evanko

RESEARCH PAPERS
Dirks, R.M. & Pierce, N.A. Triggered amplification by hybridization chain reaction. *Proc. Natl. Acad. Sci. USA* **101**, 15275–15278 (2004).

folA, encoding dihydrofolate reductase, a known drug target. Follow-up experiments confirmed that elevated bacterial expression of *folA* increased the amount of 1a or 2a needed to inhibit growth.

Brown is slightly disappointed by the extent to which efflux pumps appear to drown out target identification, but he also sees important benefits for future research. "One of the things that comes out of this paper, I think, is a way to better understand what is the substrate specificity of an efflux pump," says Brown, who indicates that his team has already learned quite a bit about how properties such as the extent of hydrophobicity might lead to increased drug efflux. His team is seeking ways to potentially identify additional targets that might be lost amid the 'noise' generated by efflux pump suppressor genes, but Brown believes that their system already has a lot to offer: "[From] eight and a half thousand molecules, we pulled out two compound-target pairs, and that's not really such a bad success rate. I think that as is, you could take this forward with much higher throughput, and I daresay that there are companies that would have the resources to do that."

Michael Eisenstein

RESEARCH PAPERS
Li, X. *et al*. Multicopy suppressors for novel antibacterial compounds reveal targets and drug efflux susceptibility. *Chem. Biol.* **11**, 1423–1430 (2004).

NEWS IN BRIEF

VIROLOGY

A novel approach for producing lentiviruses that are limited to a single round of infection

The development of lentiviral strains capable of only one round of infection is of great interest to researchers investigating the dynamics and pathogenesis of HIV and SIV. Evans *et al.* present such an SIV strain, created by mutating the ribosomal frameshifting site between the *gag* and *pol* reading frames, observing successful restriction *in vitro* and *in vivo*.

Evans, D.T. *et al. J. Virol.* **78**, 11715–11725 (2004).

MICROSCOPY

Serial block-face scanning electron microscopy to reconstruct three-dimensional tissue nanostructure

Block-face imaging offers an effective means for the generation of serial microscopic images. Denk and Horstmann apply this system in the context of environmental scanning electron microscopy, obtaining serial data that enable the high-resolution three-dimensional reconstruction of neural circuits and other nanostructures.

Denk, W. & Horstmann, H. *PLoS Biol.*, published online 19 October 2004.

CELL BIOLOGY

Mapping the dynamic organization of the nuclear pore complex inside single living cells

About 30 different nucleoporin proteins compose the nuclear pore complex, mediating transport of molecules between cytoplasm and nucleus. Rabut *et al.* have created and analyzed a series of cell lines expressing many of these proteins as GFP fusions, in an effort to better understand the *in vivo* dynamics of each different pore-complex component.

Rabut, G. *et al. Nat. Cell Biol.*, **6**, 1114–1121 (2004).

MICROARRAYS

Distinct effects on gene expression of chemical and genetic manipulation of the cancer epigenome revealed by a multimodality approach

Gius *et al.* apply a microarray strategy to characterize the impact on gene expression patterns resulting from different methods of modulating DNA methylation and find that the effects of genetic modification to eliminate DNA methyltransferase expression unexpectedly differ from those induced by drugs altering methylation or histone acetylation.

Gius, D. *et al. Cancer Cell* **6**, 361–371 (2004).

IMMUNOCHEMISTRY

Targeted gene alteration in *Caenorhabditis elegans* by gene conversion

Transposon-based mutagenesis is a popular method for *C. elegans* genetic studies, but it requires the screening of large numbers of worms, and researchers have little control over the introduced changes. Barrett *et al.* describe a combined approach using transposons and modified transgenes to efficiently introduce targeted replacements, deletions and insertions in a mutator worm strain.

Barrett, P.L. *et al. Nat. Genet.* **36**, 1231–1237 (2004).