want to screen using droplet-based microfluidics, show almost no solubility in perfluorocarbons.

Merten plans to use the system to screen for drugs that inhibit virus entry into cells. "For any cell-based assay you must guarantee that the cells survive during the assay period from a few hours to a few days," notes Merten. Their results show that cells could survive and divide for several days in a single droplet in a microfluidic device.

The tiny size of the droplets greatly reduces the amount of reagents needed for assays. "The number of viral particles we need for a 96-well plate is sufficient to screen $10^7$ samples in the droplet system," remarks Merten. "We would not be able to produce enough viral particles to perform such a screen in a microtiter plate." This nicely illustrates the value of this system for assays involving limiting reagents.

To test the limits of the system the researchers encapsulated living *Caenorhabditis elegans* worms within droplets in a small piece of tubing. A worm underwent a complete lifecycle in a droplet, showing that the droplet assay could be used for assays requiring testing of progeny.

This is just the first step on the way to using these microfluidic systems for doing high-throughput cell-based or small multicellular organism screens. So far all the droplets in the assays contain the same reagents, but Griffiths says "the next step is to establish strategies to allow us to encapsulate different drug candidates in the drops."

**Daniel Evanko**

**RESEARCH PAPERS**

Clausell-Tormos, J. *et al.* Droplet-based microfluidic platforms for the encapsulation and screening of mammalian cells and multicellular organisms. *Chem. Biol.* **15**, 427–437 (2008).

early stages of scoping out the landscape of what electrophile-nucleophile pairs you want to use," explains Cravatt. "These probes can be further tuned to be more selective for individual enzyme classes by embedding them into scaffolds that direct binding to specific targets."

Electrophilic probes, however, have the potential to target more than just enzymes. Cravatt's group noticed that one of the carbon electrophiles labeled a conserved cysteine in 3-chloride intracellular channels, opening the door to studying ion channels by ABPP.

What is next for Cravatt's team? There are thousands of proteins that we know nothing about. By generating ABPP probes directed to large classes of such unannotated proteins, they hope to begin to characterize them.

As for all of you out there hoping for that great small-molecule tool? "Unifying [ABPP] with small-molecule screening could really provide the first general method to begin to identify targets in native systems," says Cravatt. By generating ABPP probes that are subsequently embedded in the inhibitor of interest, the target(s) could be labeled in living cells, enriched and identified by LC-MS/MS. This is good cause for chemical biologists to be dancing in the streets.

**Michelle Pflumm**

**RESEARCH PAPERS**

Weerapana, E. *et al.* Disparate proteome reactivity profiles of carbon electrophiles. *Nat. Chem. Biol.*, published online 18 May 2008.

## NEWS IN BRIEF

MUTAGENESIS

### A better knockout mouse

Inducible gene targeting in mice is time-consuming and can be unreliable. Zeng *et al.* now describe an improved conditional and reversible tetracycline-based system called iKO to generate knockout mice. It boasts more tightly regulated expression of the gene of interest, powered by the gene's own promoter, so there is no need to worry about leakage or tissue specificity. This should be especially welcome news to the mouse community.

Zeng, H. *et al. PloS Genet.* **4**, e1000069 (2008).

NANOTECHNOLOGY

### Nanoparticle design

It can be quite a challenge to get nanoparticle-based delivery vehicles carrying cytosol-bound cargo through the cell membrane without doing any damage. Verma *et al.* now demonstrate that gold nanoparticles covered in alternating negatively charged and hydrophobic groups are safely delivered, whereas nanoparticles with these groups randomly distributed get stuck in endosomes. These findings are expected to be especially helpful to researchers designing gene and small interfering RNA–based therapies.

Verma, A. *et al. Nat. Mater.*, published online 25 May 2008.

GENOMICS

### Resequencing by hybridization

Competition between next-generation sequencing technologies continues to heat up. Pihlak *et al.* describe the implementation of a sequencing-by-hybridization (SBH) approach, called shotgun SBH, that solves problems of previous SBH implementations. The genomic sample is cut into fragments, immobilized on a glass surface by rolling-circle amplification and probed sequentially with universal oligonucleotides. The high throughput and low cost of the method is appealing for simple resequencing applications.

Pihlak, A. *et al. Nat. Biotechnol.* **26**, 676–684 (2008).

MICROSCOPY

### Large-scale 3D subdiffraction imaging

Many methods have been described for subdiffraction fluorescence imaging. One implementation, structured illumination microscopy (SIM), involves illumination with multiple interfering beams of structured light to double the resolution of a conventional microscope. Gustafsson *et al.* now extend SIM to imaging in three dimensions and Schermelleh *et al.* apply multicolor three-dimensional SIM to investigate the structure of the mammalian nucleus.

Gustafsson, M.G. *et al. Biophys. J.* **94**, 4957–4970 (2008).
Schermelleh, L. *et al. Science* **320**, 1332–1336 (2008).

GENOMICS

### Fruit fly CNP map

It has long been suspected that copy-number changes could be influenced by natural selection. Emerson *et al.* now present evidence of just that. Using Affymetrix genomic tiling arrays, they generated a high-resolution copy-number polymorphism map for the fruit fly. They discovered that several toxin-related genes are duplicated including the cytochrome P450 gene *Cyp6g1*, critical in conferring resistance to the insecticide dichloro-diphenyl-trichloroethane, DDT.

Emerson, J.J. *et al. Science*, published online 5 June 2008.