TOOLS IN BRIEF

MODEL ORGANISMS

GCaMP transgenic mice

Calcium imaging has proven invaluable for monitoring the activities of neuronal populations, dendrites and dendritic spines both *in vitro* and *in vivo*. These experiments are increasingly done using genetically encoded calcium indicators such as the GFP-based GCaMP family. Recently, transgenic mouse lines expressing improved versions of these indicators have been generated. Zariwala *et al.* generated a Cre-dependent reporter mouse that expresses GCaMP3. A cross of these mice with appropriate Cre mouse lines produced robust GCaMP3 expression in defined cell populations in the retina, cortex and cerebellum. Chen *et al.* report transgenic lines expressing either GCaMP2.2c or GCaMP3 under the control of the *Thy1* promoter. These mice showed GCaMP fluorescence in subsets of neurons in different brain regions and produced long-term, stable expression of the GCaMPs, with no apparent toxicity. The lines will be useful tools for long-term *in vivo* monitoring of neuronal activity.

Chen, Q. *et al. Neuron* **76**, 297–308 (2012).
Zariwala, H.A. *et al. J. Neurosci.* **32**, 3131–3141 (2012).

BIOCHEMISTRY

Measuring phosphorylation-site stoichiometry

Phosphorylation-site stoichiometry is important for understanding the functional implications of phosphorylation dynamics in the cell. However, an apparent increase in phosphorylation, for example, could simply reflect an increase in concentration of the protein of interest under a changing biological condition. It is therefore important to normalize for protein expression, but this has been challenging to do with standard western blotting. Pan *et al.* describe a functionalized, water-soluble nanopolymer reagent dubbed pIMAGO, which is used in conjunction with an antibody to measure protein phosphorylation levels with high quantitative accuracy; values are then normalized by protein concentration. pIMAGO contains titanium(IV) ions to capture phosphoproteins and infrared fluorescent dyes for high sensitivity detection. Applying pIMAGO in a microplate format, Pan *et al.* monitored spleen tyrosine kinase phosphorylation in breast cancer cell lines.

Pan, L. *et al. J. Am. Chem. Soc.* **134**, 18201–18204 (2012).

LAB-ON-A-CHIP

Probing the matrix

The deadly ability of cancers to spread depends on their complex interactions with the extracellular environment. Arrays of extracellular-matrix molecules have been used to screen for factors that determine whether cells can attach, but they are limited to testing just a handful of factors. Reticker-Flynn *et al.* now develop a large-scale, fully automated platform based on a 4,000-element polyacrylamide hydrogel–spotted array. The polyacrylamide pads can trap a wide range of molecules, allowing the researchers to measure adherence of labeled mouse lung adenocarcinoma cells to 38 matrix molecules either alone or in pairwise combinations. They found that adherence profiles of primary tumors and cells from different metastases are distinct and that the profiles depend on combinatorial interactions and correspond to molecules present at tumor sites *in vivo*.

Reticker-Flynn, N.E. *et al. Nat. Commun.* **3**, 1122 (2012).

MICROBIOLOGY

Trapping a shape-shifting bacterium

Optical trapping is a powerful tool for manipulating molecules, cells and beads. Attempts to trap and hold onto objects with changing shapes, however, have faced major technical challenges. Koch and Rohrbach now report an optical trapping approach to trap and image the rapidly shape-shifting helical bacterium *Spiroplasma*, which is of biomedical interest (it lacks a cell wall and is resistant to antibiotics). The researchers adapted the shape of the optical trapping potential to the body of the bacterium by time-sharing the laser focus. Once caught, the bacterium could be imaged with nanometer precision at up to a kilohertz rate, allowing the researchers to generate three-dimensional movies of its rapid and complex shape-shifting movements.

Koch, M. & Rohrbach, A. *Nat. Photonics* **6**, 680–686 (2012).

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