TOOLS IN BRIEF

GENOMICS

CRISPR off-target detection

Genome-editing tools, particularly transcription activator–like effector nucleases (TALENs) and the clustered, regularly interspaced, short palindromic repeats (CRISPR)-Cas9 system, are becoming increasingly widely used. But despite their popularity, questions about their off-target activity remain. Wang *et al.* present an unbiased off-target screen by tagging nuclease-created DNA double-strand breaks with integrase-defective lentiviral vectors (IDLV), which can be amplified by PCR and detected by sequencing. Whereas TALENs did not show any off-target effects when targeted to four endogenous genes, the Cas9 nuclease showed several, but these could be eliminated by the use of a Cas9 nickase. The IDLV assay can detect cleavage frequencies down to 1%, and the findings of frequent off-target sites with single-nucleotide bulges should inform the design of more specific guide RNAs for Cas9.

Wang, X. *et al. Nat. Biotechnol.* **33**, 175–178 (2015).

SENSORS AND PROBES

A nonblinking quantum dot

Quantum dots (QDs) are popular probes for imaging owing to their brightness and photostability. However, their environmental sensitivity and blinking properties limit their utility. Ji *et al.* sought to modify QDs to overcome these limitations. They encapsulated a QD first in amorphous silica and then in a gold nanoshell. The gold nanoshell serves two major functions. The first is to shield the QD from the environment, stabilizing its photophysical properties. The second is to act as a plasmonic resonator, which effectively eliminates the nonradiative processes that cause blinking. The result is a 'golden QD' that displays remarkably stable signal in single-particle spectroscopy experiments and that has higher photostability than unmodified QDs. This new class of QDs should expand the versatility of these probes for many biological applications.

Ji, B. *et al. Nat. Nanotechnol.* **10**, 170–175 (2015).

NEUROSCIENCE

Targeted electrophysiology at any depth

In studies of sparse neuronal subtypes, visual targeting of the genetically labeled neurons is an efficient way to obtain recordings of electrical activity, but this strategy is amenable to only those neurons in superficial brain layers. Muñoz *et al.* developed a method to target specific neurons in deeper brain layers with high efficiency. The researchers express the optogenetic actuator channelrhodopsin 2 in the neuronal subset of interest and randomly target neurons with a recording pipette. Once they approach a neuron, they deliver blue light via an optical fiber within the recording pipette. Evoked activity signifies that the researchers have targeted a neuron of interest, whereas they can quickly move on to another neuron if they do not observe any optogenetically induced activity.

Muñoz, W. *et al. Cell Rep.* **9**, 2304–2316 (2014).

NANOBIOTECHNOLOGY

Cell positioning with acoustic waves

In order to study cell-cell communication, researchers have been actively devising methods to precisely position cells. To date, however, such approaches have tended to perturb the cells' native state, have not achieved single-cell precision and have largely not been applicable to cells in suspension. Guo *et al.* now present a surface acoustic wave (SAW)-based technology for manipulating single cells, allowing them to be positioned with high precision. Their SAW device creates acoustic wells for entrapping cells with controlled cell-cell distance; simply changing the acoustic field enables them to change the cell assembly geometry. Cells can be cultured in their native medium and can be kept in suspension. Guo *et al.* applied the technology to study gap junctional intercellular communication by visualizing dye exchange between coupled cells.

Guo, F. *et al. Proc. Natl. Acad. Sci. USA* **112**, 43–48 (2015).