

## TOOLS IN BRIEF

## MOLECULAR ENGINEERING

**Making memories with CRISPR–Cas9**

Tracking the magnitude or duration of biological activity in mammalian cells is technically challenging. Perli *et al.* devised a strategy that uses the CRISPR–Cas9 system to store such ‘analog’ information, called mammalian synthetic cellular recorders integrating biological events (mSCRIBE). In mSCRIBE, a DNA sequence necessary for Cas9 recognition is added downstream of a gene that encodes the small guide RNA, generating a self-targeting guide RNA (stgRNA) sequence. Then the expression of Cas9 is linked to a biological process of interest. When this process occurs, the Cas9 targets the stgRNA gene for cleavage and subsequent mutagenesis during DNA repair. These mutations serve as a recording of when the process occurred. The researchers show that mSCRIBE can be used to record induced acute inflammation events over time.

Perli, S.D. *et al. Science* <http://dx.doi.org/10.1126/science.aag0511> (2016).

## BIOCHEMISTRY

**A plant metabolite spectral library**

Mass-spectrometry-based studies aimed at the discovery of small-molecule metabolites in biological systems rely on the use of spectral libraries for interpretation of experimental spectra. These libraries are generated using authentic standard compounds. But such spectral libraries, especially those covering plant metabolites, are woefully incomplete; as a result, only a very small fraction of the total estimated number of metabolites can be identified in metabolomics studies. Shahaf *et al.* now present WEIZMASS, a spectral library generated from high-resolution mass spectrometry data for 3,540 structurally diverse plant metabolites. They also describe MatchWeiz, a software tool used to match experimental spectra to the library spectra for identification. Using this approach, the researchers identified metabolites in three plant species from the Lemnaceae family, the tomato plant, and the model plant *Arabidopsis*.

Shahaf, N. *et al. Nat. Commun.* **7**, 12423 (2016).

## SYSTEMS BIOLOGY

**A yeast global genetic interaction map**

The synthetic genetic array approach is used to identify genetic interactions in the yeast *Saccharomyces cerevisiae*. In this method, double mutants are constructed and evaluated for fitness. If fitness is greater than expected, the genetic interaction is classified as positive; if fitness is poorer than expected, the genetic interaction is classified as negative (often the two genes code for proteins in the same complex or process). Costanzo *et al.* now present a global genetic interaction network for yeast, covering nearly all ~6,000 yeast genes. By constructing more than 23 million double mutants, they identified ~350,000 positive and ~550,000 negative pairwise genetic interactions. This ultra-dense map, illustrating the functional architecture of the yeast cell, should serve as an important resource for studying the relationships between genes, and it may also be useful for drug discovery.

Costanzo, M. *et al. Science* **353**, aaf1420 (2016).

## SENSORS AND PROBES

**Monomeric near-infrared fluorescent proteins**

Near-infrared fluorescent proteins (NIR FPs) derived from bacterial phytochromes are useful for a broad range of applications, including multicolor and deep-tissue imaging. Scherbakova *et al.* developed three monomeric NIR FPs, called miRFPs, that have desirable photophysical properties and perform well in diverse applications. The researchers demonstrate that the spectrally distinct miRFPs, which emit maximally at 670, 703 and 709 nm, respectively, are twofold to fivefold brighter than existing monomeric NIR FPs and have bright signal at endogenous levels of the cofactor biliverdin. To demonstrate their broad applicability, the researchers showed that the miRFPs can perform well in multiple fusions for determining subcellular localization, and that they are useful for structured illumination microscopy. They also used the miRFPs to develop reporters based on bimolecular fluorescence complementation and for *in vivo* imaging in mice.

Scherbakova, D.M. *et al. Nat. Commun.* **7**, 12405 (2016).