RESEARCH HIGHLIGHTS

TOOLS IN BRIEF

GENETICS

Forward genetics in nonmodel species

The field of genetics was founded on the principle of 'break it and find out what went wrong'. Mutation mapping—finding out what went wrong—has historically been the difficult part of genetic screening. Mapping by recombination-based methods is, happily, being replaced by faster methods that compare whole genome sequences, but these approaches rely on resequencing a reference genome. Nordström *et al.* avoid the need for a reference by finding changes in overlapping subsequences of sequence reads, known as *k*-mers, that are uniquely present in an affected individual and absent in an unaffected close relative. Their 'needle in the *k*-stack' (NIKS) algorithm identified candidate homozygous mutations in genetic screens of rice cultivars and alpine rockcresses. Examining backcrossed mutants allowed the authors to unambiguously identify causal mutations in nonrepetitive regions of the genome.
Nordström, K.J.V. *et al. Nat. Biotechnol.* **31**, 325–330 (2013).

NEUROSCIENCE

Metabotropic receptors under the spotlight

Metabotropic glutamate receptors (mGluRs) play important roles in synaptic transmission between neurons. To develop tools for manipulating the function of specific mGLuRs in cells and tissues, Levitz *et al.* used an optochemical approach combining synthetic photoswitchable tethered ligands (PTLs) and engineered versions of the receptor. Using this strategy, they generated light-activated and light-inhibited versions of mGluR2 (LimGluRs). LimGluR2, when covalently bound by the PTL, becomes activated by a 380-nm light pulse and deactivated by a 500-nm pulse. In contrast, LimGluR2-block is inactivated when illuminated at 380 nm by the action of its PTL, which blocks binding of the endogenous ligand glutamate, and this inactivation is reversed at 500 nm. The tools trigger the same downstream signaling pathways as those of the endogenous mGluRs, and a single photoswitch is enough to keep them turned on or off as long as desired.
Levitz, J. *et al. Nat. Neurosci.* **16**, 507–516 (2013).

BIOINFORMATICS

Biological models in Python

An increasing number of research studies are combining experimental measurements of a particular process or phenomenon with mathematical models of it, frequently toggling between the two to yield a detailed quantitative understanding. Such models are typically written as equations, which can be difficult and tedious to modify without error or to share. Lopez *et al.* now describe an open-source framework, PySB, in which the biological models are Python programs. PySB is interoperable with the rule-based languages BioNetGen and Kappa. The resulting models will benefit from popular Python tools for documentation, analysis, visualization and sharing.
Lopez, C.F. *et al. Mol. Sys. Biol.* **9**, 646 (2013).

SYSTEMS BIOLOGY

Profiling ubiquitin-like modifications

Post-translational modification of proteins with ubiquitin and ubiquitin-like (Ubl) modifications has a substantial impact on protein function, stability, interactions and localization. Though ubiquitination is fairly well studied, much less is known about the functions and protein targets of other Ubl modifications. Merbl *et al.* now present an extensive resource, profiling the ubiquitin and six Ubl modification targets—including SUMO1, SUMO2/3, NEDD8, UFM1, FAT10 and ISG15—during mitosis. They used a previously reported protein microarray–based approach to probe active, concentrated cell extracts, detecting Ubl modifications on the spotted proteins using Ubl modification–specific antibodies. In total they identified 1,500 putative substrates; about 35% of protein targets were subject to alteration by multiple Ubl modifications, but about 80–200 targets were unique to each Ubl modification profiled. The resource provides a valuable map for detailed biological follow-up experiments.
Merbl, Y. *et al. Cell* **152**, 1160–1172 (2013).