TOOLS IN BRIEF

GENOMICS

Expanding the range of base editors

The use of the Cas9 nickase fused to cytidine deaminases such as APOBEC1 has achieved great success in converting C to T nucleotides. But Cas9 relies on an NGG protospacer-adjacent motif (PAM) sequence to bind its target, which limits its target range. Li *et al.* expanded the genome-wide reach of base editors (BEs) by fusing APOBEC1 to catalytically inactive Cpf1, which recognizes TTTA/C/G sequences. The optimized dCpf1-BE from *Lachnospiraceae bacterium*, which also included a nuclear localization signal and a uracil DNA glycosylase inhibitor, achieved editing rates of 44% in a plasmid-based reporter system and up to 37% in selected targets in human cells. The researchers assessed 40 predicted off-target sites for eight guide RNAs and found that dCpf1-BE showed activity at only three sites for one guide RNA. Further improvements to Cpf1 to narrow the editing window and expand recognition to different PAMs are in the works.

Li, X. *et al. Nat. Biotechnol.* **36**, 324–327 (2018).

STRUCTURAL BIOLOGY

*cis*TEM software for cryo-EM

The rapidly growing interest in cryo-electron microscopy (cryo-EM), driven by major technological advances in recent years, has increased the demand for powerful yet user-friendly software tools. Grant *et al.* present *cis*TEM (computational imaging system for transmission electron microscopy), a complete software solution for single-particle cryo-EM data analysis, from raw image processing to structure determination. *cis*TEM was built from existing and novel algorithms that implement essential steps such as movie processing, image defocus determination, particle picking, 2D classification, 3D map generation, and 3D refinement. This open-source software program is designed to run on high-end CPU workstations and contains an easy-to-use graphical user interface. Grant *et al.* demonstrate the performance of *cis*TEM, using β-galactosidase as an example.

Grant, T. *et al. eLife* **7**, e35383 (2018).

SENSORS AND PROBES

GFP goes sour

Fluorescent proteins such as GFP are invaluable for imaging proteins. However, the acidic environment in organelles of the secretory pathway is not conducive for many fluorescent proteins, especially those of the green variety. Shinoda *et al*. have discovered a new GFP from the jellyfish *Olindias formosa* that has limited sequence homology to other GFPs. In contrast to available GFPs, the new variant turned out to be highly acid tolerant. Via both rational design and directed evolution, the researchers monomerized the original protein and increased its solubility and brightness to generate the final GFP, which they called Gamillus. Gamillus is about half as bright as EGFP in HeLa cells and performs well in a variety of fusion proteins. Importantly, Gamillus retains its fluorescence in lysosomes and should therefore be a useful tool for studying the secretory pathway.

Shinoda, H. *et al. Cell Chem. Biol.* **25**, 330–338 (2018).

MICROBIOLOGY

Metabolomes from metagenomics and modeling

Metabolic profiling of microbial environments such as the human gut has lagged behind surveys of genetic material, which are generally cheaper and less challenging to carry out. Shotgun metagenomic sequencing provides quantitative information about what genes are present in a community, but it is not straightforward to predict metabolic status from these data. To bridge the gap, Garza *et al*. introduce MAMBO (metabolomic analysis of metagenomes using flux balance analysis and optimization), which assesses and optimizes correlations between genome-scale, constraint-based metabolic models and microbial abundance profiles obtained from shotgun sequence data. MAMBO inference of the metabolomics environment for several human body sites is consistent with measured metabolomes, which provides support for the approach as a step toward mechanistic modeling of microbial ecology.

Garza, D.R. *et al. Nat. Microbiol.* **3**, 456–460 (2018).