TOOLS IN BRIEF

IMAGING

Refractive index matching in living samples

Mismatches in refractive index (RI) between biological specimens and their surrounding media can lead to problems during imaging such as spherical aberrations that negatively impact image quality and fidelity. These aberrations are often worse for thick and complex samples and can hinder deep imaging. Boothe *et al.* developed an approach to correct for RI mismatches in live imaging. Their approach involved identifying a chemical compound with high water solubility and low toxicity with a high RI that could be mixed with sample media to tune the RI of the media. The compound they identified and demonstrated to meet these criteria was Iodixanol. They found that Iodixanol has low toxicity on a number of samples, including developing zebrafish, and that RI matching with Iodixanol improves image resolution and signal-to-noise at greater tissue depths.

Boothe, T. *et al. eLife* **6**, e27240 (2017).

CHEMICAL BIOLOGY

A chemical genetic screening system for yeast

Chemical probes are valuable tools for studying protein function. Identifying the mechanisms of action of such compounds, however, is a major challenge. Piotrowski *et al.* report a high-throughput platform for screening for chemical probe function in yeast. The platform is based on the idea that if a compound targets a particular protein, this activity should resemble the genetic interaction profile resulting from loss-of-function mutations in the corresponding gene. The researchers created a set of barcoded yeast gene-deletion mutants in a drug-sensitized background, and then they used highly multiplexed barcode sequencing to simultaneously generate chemical genetic interaction profiles for hundreds of compounds. They compared these chemical genetic interaction profiles with available genetic interaction profiles to predict compound target pathways. This approach enabled them to screen more than 13,000 compounds and yielded functional information for 1,522 probes.

Piotrowski, J.S. *et al. Nat. Chem. Biol.* http://dx.doi.org/10.1038/nchembio.2436 (2017).

MICROSCOPY

Tools for mining microscopy data

High-throughput and high-content microscopy data are invaluable for biological research, yet they are generated at a scale that can preclude fully manual interrogation. A number of algorithmic tools, such as machine-learning approaches, have been developed for semiautomated or fully automated assessment of large image data sets. Piccinini *et al.* describe a second version of their Advanced Cell Classifier software package for phenotypic analysis of large-scale, cell-based microscopy experiments. The software is meant to provide a user-friendly package to facilitate training machine-learning algorithms and mine data to classify cells, discover new and/or rare phenotypes, and improve the accuracy of the analysis process. The software package was validated on synthetic and experimental data, and it should prove useful for researchers working in high-content imaging.

Piccinini, F. *et al. Cell Syst.* **4**, 651–655.e5 (2017).

MOLECULAR ENGINEERING

Affimers as research reagents

Antibodies are essential research tools across biology, but problems with antibody specificity, reproducibility, and characterization are prevalent, not to mention the drawbacks associated with traditional animal-based methods for generating antibodies. Recombinantly produced binder proteins, such as the Affimer scaffold, are promising alternatives. These reagents can be rapidly selected and expressed in *Escherichia coli* or mammalian cells, and they target proteins and even small molecules with high affinity, specificity, and stability. Tiede *et al.* demonstrate that Affimer antibody mimetics are useful in multiple research applications, such as for pull-down of specific Src-Homology 2 (SH2) domains, function blocking of VEGFR2 and the ion channel TRPV1, *in vivo* staining of tenascin C, affinity fluorescence of the herpes virus of turkeys protein UL49, super-resolution imaging of the cancer-related HER4 receptor, and even for detection of the explosive organic molecule trinitrotoluene (TNT).

Tiede, C. *et al. eLife* **6**, e24903 (2017).