IN BRIEF

GENOMICS

A winning single-cell combination

Cao, J. et al. *Science* **361**, 1380–1385 (2018).

It has recently become possible to interrogate multiple molecular classes from an individual cell, yet this achievement is typically low throughput. Cao et al. now use single-cell combinatorial indexing to jointly profile gene expression and chromatin accessibility from large numbers of cells. In their sci-CAR method, pooled nuclei are distributed in wells, and well-specific barcodes are incorporated in first-strand cDNA and delivered to genomic regions by Tn5 transposition. Mixing and redistribution of intact nuclei allows a new well-specific barcode to be added to second-strand cDNA and genomic fragments during amplification, such that all molecules receive the unique barcode combination corresponding to their nucleus of origin. The authors sequenced thousands of cells from mouse kidney and three time points of a dexamethasone-treated cancer cell line, and were able to classify cell types, observe accessibility and expression dynamics, and link regulatory regions with target genes. *TN*

https://doi.org/10.1038/s41592-018-0197-6

CELL BIOLOGY

Smarter cell sorting

Nitta, N. et al. *Cell* **175**, 266–276 (2018).

The ability to rapidly separate phenotypically different cells at high throughput could offer major advantages for understanding the function and behavior of various cell types and cell states. However, accurate sorting often requires high-content information, and processing of this information to distinguish populations is often slow. To bypass these limitations, Nitta et al. developed a machine-learning-based approach for extremely rapid classification of cells during imaging flow cytometry, thus enabling 'intelligent image-activated cell sorting' with high speed and accuracy. Their system integrates microscopy, microfluidics, instrument control hardware and software, and deep-learning-based image analysis for real-time sorting. They highlight the power of the approach by demonstrating the sorting of microalgal and blood cells on the basis of subcellular protein localization and intercellular interactions. *RS*

https://doi.org/10.1038/s41592-018-0198-5

IMAGING

Shaking up clearing cocktails

Tainaka, K. et al. *Cell Rep.* **24**, 2196–2210 (2018).

Tissue-clearing technologies improve optical access to scattering tissue such as brain. Although a number of different approaches are available, their development typically has been serendipitous and did not necessarily follow a rational strategy. Tainaka et al. screened a collection of about 1,600 hydrophilic chemical compounds for favorable performance in delipidation, decolorization, refractive index matching and decalcification assays. The researchers then combined promising compounds into several different CUBIC (clear, unobstructed brain/body imaging cocktails and computational analysis) cocktails designed to achieve good performance in bone clearing, human brain clearing, or fast clearing, or to preserve fluorescence in tissues expressing fluorescent proteins. The various CUBIC cocktails can be mixed and matched in accordance with experimental needs. The researchers demonstrated their updated CUBIC protocols by clearing whole mice, large human tissue samples, and a marmoset brain. *NV*

https://doi.org/10.1038/s41592-018-0199-4

PROTEOMICS

Finding S-sulfinylated proteins

Akter, S. et al. *Nat. Chem. Biol.* https://doi.org/10.1038/s41589-018-0116-2 (2018).

The amino acid cysteine undergoes many different oxidative post-translational modifications involved both in disease and in the regulation of various biological functions. S-sulfinylation is a particularly elusive modification that has been a biochemical challenge to study, and its biological function has thus remained unresolved. Akter et al. now report a clickable, electrophilic diazene probe called DiaAlk, which allows them to enrich for proteins containing sulfinic acid modifications. The probe facilitates mass-spectrometry-based identification of such modified proteins, or fluorescence-based detection in cells. The researchers used DiaAlk in several applications, including analysis of cysteines in A549 or HeLa cells that had undergone hyperoxidation after the addition of hydrogen peroxide. The approach also enabled them to compare the targets of S-sulfinylation with those of S-sulfenylation, and to identify protein substrates of the cysteine sulfinic acid reductase sulfiredoxin in mouse embryonic fibroblasts. *AD*

https://doi.org/10.1038/s41592-018-0200-2