IN BRIEF

MICROSCOPY

Deeper imaging with space gating

Jang, M. et al. *Nat. Commun.* **11**, 710 (2020).

Imaging at depth within biological specimens is a long-standing goal of optical microscopy. However, such deep-tissue imaging is limited by light interacting with the specimen, which leads to light scattering. 'Gating' strategies, which are effective at filtering out multiply scattered waves, have been developed to bypass these limitations. Jang et al. present a complementary gating approach called space gating, which is based on interferometric detection schemes developed for photoacoustic imaging. Space gating is applied at the object plane and uses selective measurement of the ballistic wave that is modulated by a high-frequency ultrasound focus as small as ~30 µm × 70 µm. Space gating allows effective filtering of multiply scattered waves that cannot be filtered out with existing approaches. The researchers demonstrate the power of space-gated microscopy with quantitative phase imaging of cells embedded in scattering medium and skeletal muscle structure in intact zebrafish 30 days post-fertilization. *RS*

https://doi.org/10.1038/s41592-020-0808-x

GLYCOBIOLOGY

Smart anti-glycan reagents

McKitrick, T. R. et al. *Commun. Biol.* **3**, 91 (2020).

Glycans play a crucial role in a variety of biological processes, yet their high structural diversity makes biological studies on glycan expression very difficult. A fundamental bottleneck is lack of reliable reagents that bind in a highly specific, structure-dependent manner. McKitrick et al. have developed a platform based on the unusual immune system of the sea lamprey to identify such reagents. Upon exposure to immunogens, these organisms secrete circulating antigen-specific variable lymphocyte receptor B (VLRB) antibodies, which have similar combinatorial diversity to that of the human antibody repertoire. Diverse sets of glycan immunogens were used to generate VLRBs, and the expressed VLRBs were screened for specificity using a microarray consisting of ~600 unique glycan structures. The characterized VLRBs with unique glycan specificity are termed smart anti-glycan reagents (SAGRs). The authors report 15 SAGRs that can discriminate among linkages, functional groups and unique glycan motifs. *AS*

https://doi.org/10.1038/s41592-020-0809-9

GENE EXPRESSION

Microbial factory for crRNAs

Jiang, W. et al. *Cell* **180**, 1002–1017 (2020).

Genome-wide CRISPR screens are a powerful tool for revealing gene functions. Yet the synthesis of guide RNA libraries can be expensive and time consuming. Jiang et al. leverage naturally occurring CRISPR–Cas adaptation machinery to convert exogenous DNA into CRISPR RNA (crRNA) libraries in bacteria. More specifically, they transform *Staphylococcus aureus* cells with sheared genomic DNA of interest via electroporation, which generates genome-wide crRNA libraries. These libraries can be subcloned into other species or directly used in *S. aureus*; the latter circumvents cloning and transformation steps. When cells were electroporated with *Escherichia coli* DNA, the resulting library covered over 4,000 genes with an average of 103 crRNAs per gene. In a CRISPR interference screen, the crRNA libraries were subcloned into *E. coli* and used to survey a range of transcriptional repression, leading to an identification of new antibiotic-potentiating pathways. *LT*

https://doi.org/10.1038/s41592-020-0810-3

PROTEOMICS

Quantitative proteomics of cancer cell lines

Nusinow, D. P. et al. *Cell* **180**, 387–402 (2020).

The Cancer Cell Line Encyclopedia (CCLE) is a catalog of nearly 1,000 human cancer cell lines that have been extensively profiled. Over the past decade data from gene expression, histone profiling, RNA-seq, DNA methylation, microRNA profiling, whole-genome sequencing, metabolite profiling and drug sensitivity screens have been added. In spite of extensive analyses, large-scale proteomics profiling data of human samples across such a diverse population are missing. Nusinow et al. have performed quantitative protein expression profiling of 375 cell lines distributed over 22 lineages in the CCLE, using mass spectrometry. This dataset allowed the researchers to analyze the proteome in microsatellite-instable colorectal cancers that display orders of magnitude more mutations than other tumors, revealing dysregulation of certain protein complexes associated with surveillance of mutation and translation. The resource will allow further exploration of other cancer types and non-cancer cellular processes. *AS*

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