CHEMICAL BIOLOGY

Proximity labeling with TurboID

Branon, T. C. et al. *Nat. Biotechnol.* **36**, 880–887 (2018).

Enzyme-catalyzed proximity labeling has rapidly become a popular approach for studying the spatial localization and interactions of proteins in the cell. In this technique, a protein of interest is labeled with a promiscuous enzyme that adds a tag such as biotin to near-neighbor proteins, thereby enabling their purification and identification by mass spectrometry. Although several systems are now available, the most commonly used approaches are APEX, which uses an ascorbate peroxidase and offers rapid tagging kinetics but is limited by the requirement for toxic hydrogen peroxide addition, and BioID, based on a nontoxic biotin ligase system, which has slow tagging kinetics. Branon et al. now report a system that allows rapid nontoxic proximity labeling in just 10 minutes. Using yeast display, they evolved the *Escherichia coli* biotin ligase BirA to generate new promiscuous tagging variants, which they dubbed TurboID and miniTurbo. The researchers demonstrate that the TurboID system is applicable in organisms including worms and flies. *AD*

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MICROSCOPY

Gentler super-resolution microscopy

Masullo, L. A. et al. *Nat. Commun.* **9**, 3281 (2018).

Super-resolution microscopy is often considered challenging to apply to living specimens because of the high, potentially toxic light doses and long collection times typically used to generate images. Masullo et al. addressed this challenge by developing the 'molecular nanoscale live imaging with sectioning ability' (MoNaLISA) nanoscope for prolonged super-resolution imaging with relatively low light intensities. MoNaLISA is conceptually similar to reversible saturable optical fluorescent transition (RESOLFT) microscopy, but it overcomes the limitations of that approach by using light patterns with optimized shapes and periodicities to control the reversibly switchable fluorescent proteins used for labeling. The result is a microscopy method that achieves ~50-nm resolution over entire cell volumes over long periods. The researchers demonstrated the approach for time-lapse imaging of organelles, colonies of mouse embryonic stem cells, and neurons. *RS*

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SYNTHETIC BIOLOGY

Engineering wild bacteria

Brophy, J. A. N. et al. *Nat. Microbiol.* **3**, 1043–1053 (2018).

Undomesticated bacteria have a very wide range of properties that could be exploited for research, medicine, and technology with some engineering, but most of the bacteria in the wild are difficult if not impossible to genetically manipulate. To address this, Brophy et al. take advantage of conjugation, the natural process of DNA transfer between bacteria that secretes a protein–DNA complex from a donor to a recipient cell. They designed a *Bacillus subtilis* strain, XPORT, with a mobile integrative and conjugative element (ICE) and used it to transfer heterologous DNA to a recipient strain, ensuring that it could not spread beyond that strain. The approach allowed engineering of 52 species and 17 genera of bacteria, including isolates from human gut and skin. To illustrate a practical application, the researchers introduce a nitrogen-fixation pathway into various host bacteria. *NR*

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BIOCHEMISTRY

Large-sized bilayer nanodiscs

Zhao, Z. et al. *J. Am. Chem. Soc.* **140**, 10639–10643 (2018).

Phospholipid-bilayer nanodiscs are model membrane systems that offer a native-like environment for the study of membrane proteins. However, the size of such synthetic bilayer nanodiscs is generally limited to less than 20 nm in diameter, which hinders their application with large membrane proteins. To address this limitation, Zhao et al. used a DNA origami scaffold to assist in the formation of stable nanodiscs with a diameter of ~70 nm. They used a DNA origami barrel as a scaffolding corral to recruit a number of small (~11 nm) nanodiscs, and then used detergent to induce local rearrangement of the adjacent bilayers, thus allowing neighboring nanodiscs to merge and form one interconnected structure. The flexibility of the DNA origami scaffold and excess lipids are required for the formation of large, circular, bilayer nanodiscs. The enclosed nanodiscs are relatively stable and tolerant to a broad range of pH levels and divalent ion concentrations. The researchers applied this nanodisc system to reconstitute two membrane-protein clusters and to study poliovirus entry. *LT*

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