IN BRIEF

PROTEOMICS

Comprehensive mapping of ubiquitination

Akimov, V. et al. *Nat. Struct. Mol. Biol.* **25**, 631–640 (2018).

Current approaches to enrich ubiquitinated proteins for analysis and identification by mass spectrometry suffer from various limitations. For example, ubiquitin binding domains successfully capture modified proteins, but do not provide information about ubiquitination sites. A popular approach that uses an antibody to detect a diglycine remnant of ubiquitin left over after tryptic digestion shows some bias toward certain sequences and is unable to distinguish ubiquitination from other ubiquitin-like protein modifications. Akimov et al. describe a new approach that uses an antibody dubbed UbiSite, which recognizes a 13-amino-acid remnant, specific to ubiquitin, left on ubiquitinated proteins after digestion with the protease LysC. Using proteasomal inhibitors and UbiSite-based enrichment, the researchers identified more than 63,000 ubiquitination sites on more than 9,000 proteins in human Hep2 and Jurkat cell lines. They found that ubiquitination was widespread, affecting proteins involved in all cellular processes in all locations in the cell. *AD*

https://doi.org/10.1038/s41592-018-0122-z

IMMUNOLOGY

CRISPR and immunity

Wienert, B. et al. *PLoS Biol.* **16**, e2005840 (2018).

The use of in vitro transcribed (IVT) single guide RNAs, complexed with Cas9, has improved CRISPR-mediated gene editing in primary cells such as T cells, hematopoietic stem cells and neurons. What is less well explored is the cells' reaction to this foreign RNA. Cells defend themselves against RNA viruses with an innate immune response that recognizes the RNA and triggers a signaling cascade leading to the expression of type I interferon, which causes cell stress and even death. Wienert et al. tested the effect of IVT sgRNAs in several human cell types. They found a dramatic increase in interferon-β transcription even with sgRNA concentrations as low as 1 nM, and noted that this effect could be ameliorated by the removal of the sgRNA's 5′ triphosphate. The researchers recommend that bulk edited cells be checked for type I interferon expression. They also caution that because interferon can be secreted and sensed by surrounding cells, widespread innate immune responses could be triggered in a tissue by a few edited cells. *NR*

https://doi.org/10.1038/s41592-018-0123-y

NEUROSCIENCE

Expansion of the transgenic toolkit in mouse

Daigle, T. L. et al. *Cell* **174**, 465–480 (2018).

Cre driver lines and Cre-dependent reporters are important tools for studying the anatomy and function of the mouse brain. Daigle et al. now add 49 mouse lines to the existing collections of tools. About half of these lines are Cre and Flp lines with verified expression in various neuronal populations of interest. The remaining lines harbor reporters that are integrated into either the Rosa26 or the TIGRE locus. To achieve high reporter expression, the TIGRE tools rely on a tTA2-based amplification loop. Reporter lines based on the previously reported TIGRE1.0 platform require two sequential crosses with two driver lines, whereas the newly established TIGRE2.0 platform relies on a single cross only. The reporters include fluorescent proteins, calcium sensors and voltage sensors, as well as tools such as channelrhodopsin variants. These mouse lines represent a substantial addition to the existing mouse genetic toolkit and will facilitate genetic manipulations for the mouse neuroscience community. *NV*

https://doi.org/10.1038/s41592-018-0124-x

NEUROSCIENCE

The whole fly brain in detail

Zheng, Z. et al. *Cell* **174**, 730–743 (2018).

Whole-brain electron microscopy (EM) datasets are available for a few select organisms and have proven invaluable for researchers attempting to gain a better understanding of the neuronal circuitry. Zheng et al. report an EM dataset of an adult female *Drosophila* brain at synaptic resolution. The team cut about 7,000 serial sections, imaged them with transmission EM and assembled them into a high-quality volume reconstruction. For efficient imaging, the researchers used either transmission EM camera arrays or an automated sample-loading system in combination with a regular transmission EM system. To ascertain the quality of the acquired data, they manually traced neurons in the mushroom body, an olfactory memory center in the fly brain, and found that the reproducibility between independent tracings of the same neurons was high. Furthermore, the traced neurons could be aligned to neurons reconstructed on the basis of light microscopy images. The whole-brain dataset is freely available for use in further studies. *NV*

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