NEUROSCIENCE

A photoswitch for modulating neuronal activity

DiFrancesco, M. L. et al. *Nat. Nanotechnol.* https://doi.org/10.1038/s41565-019-0632-6 (2020).

A wide variety of azobenzene-based photoswitches have been developed for manipulating the activity of, for example, enzymes or receptors. Photoswitching involves the light-dependent *trans*→*cis* isomerization of the azobenzene moiety of the photoswitch molecule. The resulting conformational change modulates the activity of the target protein, molecule or structure. DiFrancesco et al. developed a photoswitch, called Ziapin2, that modulates membrane properties in response to blue light. Ziapin2, with amphiphilic properties, readily integrates into cell membranes, with a preference for lipid rafts. In the dark, Ziapin2 in the *trans* configuration leads to thinning of the membrane, which increases membrane capacitance. Upon illumination, membranes revert to their original state and hyperpolarize, which is followed by a rebound depolarization. When Ziapin2 is used in neurons, illumination elicits action potentials. DiFrancesco et al. demonstrate that Ziapin2 can be applied in vivo, where they elicit activity in the mouse somatosensory cortex upon loading with Ziapin2 and illumination. *NV*

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NEUROSCIENCE

Beware the unexpected in Cre drivers

Luo, L. et al. *Neuron* https://doi.org/10.1016/j.neuron.2020.01.008 (2020).

The Cre–*loxP* system allows temporal and/or spatial control over reporter gene expression in model organisms, particularly the mouse. But all is not well with this tool: undesirable expression patterns can appear. Such problems can arise from unwanted germline expression of the Cre recombinase. Alternatively, mosaic expression of the Cre driver can complicate genotyping. In addition, recombination can be more or less efficient, depending on the floxed locus. Luo et al. have analyzed the rates of germline recombination in two commonly used Cre mouse lines and collected similar data for a broad selection of additional Cre lines widely used in the neuroscience community. The researchers recommend breeding strategies to deal with these problems and provide additional guidelines. Finally, the phenomenon is not restricted to mice but can also be observed in zebrafish Cre lines. *NV*

https://doi.org/10.1038/s41592-020-0815-y

MICROSCOPY

Selective volume illumination microscopy

Truong, T. V. et al. *Commun. Biol.* **3**, 74 (2020).

Light-field fluorescence microscopy (LFM) has benefits for fast volumetric imaging because it is able to capture an extended sample volume in a single image. LFM uses a microlens array at the sample plane to capture the light field coming from a sample on a 2D camera. The 3D distribution of fluorescent emitters within the sample can then be determined through computational reconstruction of the 2D image. Despite the benefits, LFM can suffer from limited contrast, in part because it uses wide-field illumination, which excites regions outside the volume of interest. Truong et al. have developed selective volume illumination microscopy (SVIM), which overcomes this limitation by using light sheet illumination. The authors showcase the benefits of SVIM, which include fast, high-contrast, single-cell-resolution imaging, by imaging challenging biological samples, including bacteria flowing in seawater as they colonize a squid, the beating heart of larval zebrafish, and neural activity in larval zebrafish. *RS*

https://doi.org/10.1038/s41592-020-0812-1

GENE EXPRESSION

Guide RNA resource for *Drosophila*

Port, F. et al. *Elife* **9**, e53865 (2020).

CRISPR screens have become a valuable tool for interrogating gene function in mammalian cells. In vivo CRISPR screens typically rely on tight temporal and spatial control of mutagenesis, which remains a challenge. Port et al. describe and characterize a single guide RNA (sgRNA) library for tissue-specific CRISPR screening in *Drosophila*. Currently, tissue-specific expression of transgenes is often enabled by the Gal4–UAS system in *Drosophila*. In this work, the researchers use UAS-Cas9 transgenes and a sgRNA expression vector (pCFD6) to attain Gal4-dependent CRISPR mutagenesis. They demonstrate this conditional CRISPR mutagenesis in somatic tissues, such as imaginal discs, and in the germline. Overall, the resource consists of around 2,600 plasmids and 1,700 fly lines, mainly covering functional gene groups such as kinases, phosphatases and transcription factors. These transgenic fly lines and the plasmids will be publically available. *LT*

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