TOOLS IN BRIEF

GENOMICS

Improving CRISPR-induced homologous recombination

For precise modification of a genome—for example, to add a tag or replace one gene with another—homology-directed repair (HDR) is needed. The clustered, regularly interspaced, short palindromic repeats (CRISPR) system induces targeted double-strand DNA breaks that can then be repaired with an exogenous DNA donor, but the efficiency of this process is low. Maruyama *et al.* reasoned that the inhibition of the more frequent repair pathway, nonhomologous end joining (NHEJ), in which a break is repaired without insertional mutagenesis, would increase the efficiency of HDR. They inhibited a DNA ligase essential for NHEJ and showed an increase in HDR efficiency in cell lines and in mice derived from zygotes injected with the CRISPR components and donor DNA.

Maruyama, T. *et al. Nat. Biotechnol.* doi:10.1038/nbt.3190 (23 March 2015).

NEUROSCIENCE

Intersectional tools for mouse neuroscience

Genetic targeting is a reliable strategy to manipulate or record neural activity *in vivo*. Madisen *et al.* expand the toolkit available to researchers working on the mouse brain by establishing the TIGRE locus as a docking site for transgene insertion. This development represents a standardized platform for the expression of reporters or drivers for neural manipulations. The researchers also generated tools for intersectional targeting strategies that rely on Dre or Flp recombinases, or on the transcriptional activator tTA, in addition to Cre recombinase. With these approaches, expression patterns can be refined better than with traditional targeting strategies with a single recombinase. To complement these targeting approaches, the researchers generated a number of compatible reporter lines for fluorescent labeling, calcium or voltage sensing, or optogenetic manipulation.

Madisen, L. *et al. Neuron* **85**, 942–958 (2015).

CHEMICAL BIOLOGY

Photocages activated by green light

Photoremovable protecting groups, or photocages, are molecules that are covalently linked to a target molecule to inhibit its activity. Upon application of light treatment, the target molecule is released from the caged structure, thus activating its function. Photocages have become widely used in biological research. However, most are limited in terms of applications because they absorb ultraviolet light, which does not penetrate deeply into tissues and which can cause phototoxicity. Goswami *et al.* describe new BODIPY (boron-dipyrromethene)-based photocages that are activated with green light. They identified these photocages using a computational screening approach and showed that the photocages are functional in living *Drosophila* S2 cells. These new tools should provide a useful alternative to *o*-nitrobenzyl photocaging systems.

Goswami, P.P. *et al. J. Am. Chem. Soc.* **137**, 3783–3786 (2015).

STEM CELLS

Lung organoids

Stem cells can be directed to take different fates and, in some cases, to form complex three-dimensional (3D) structures with features of intact organs *in vitro*. Previous work showed that when FGF and WNT signaling is stimulated, endoderm derived from human pluripotent stem cells will self-organize into 3D spheroids containing mesenchymal and polarized epithelial cells. Dye *et al.* demonstrate that inhibiting BMP while stimulating HH signaling during this process generates lung organoids that can subsequently be expanded robustly in FGF10 medium. The organoids include cell types of the proximal lung epithelium surrounded by mesenchymal tissue and generate airway-like structures. RNA sequencing analysis showed that the organoids strongly resemble human fetal lung and may therefore serve as a tool for the study of lung development and disease.

Dye, B.R. *et al. eLife* **4**, e05098 (2015).