TOOLS IN BRIEF

MODEL ORGANISMS

Colorful mosaic gene-function analysis in mice

Mosaic genetic analyses are widely used in *Drosophila* to study gene function in a cell-autonomous or tissue-specific fashion. Such analyses are less easily conducted in mice. Pontes-Quero *et al.* report tools to generate mosaic mice efficiently and relatively quickly. Their inducible, fluorescent, and functional genetic mosaic (ifgMosaic) strategy is inspired by the Brainbow technology and relies on the mutually exclusive expression of three sets of fluorescent reporters and genes of interest from a single construct. The construct is available with either membrane-bound or nucleus-targeted fluorescent reporters. When combining the two constructs in the same mouse, in principle up to six genes can be studied in up to 15 distinct clonal combinations. To facilitate generation of the mosaic mice, the researchers report efficient cloning and transgenesis strategies. The ifgMosaic approach is applied to study the Notch and VEGF pathways during neurogenesis and angiogenesis.

Pontes-Quero, S. *et al. Cell* **170**, 800–814.e18 (2017).

GENOMICS

Know thine inbred mouse

In the last 100 years, the number of inbred mouse strains has grown to over 500. While C57BL/6J is the best characterized strain, many other strains serve to address particular research questions. In assessing the connection between genotype and phenotype, it is important to understand how the genetic background in a particular strain affects the penetrance of a mutation. To facilitate a user-friendly search of 36 inbred mouse strains, Timmermans *et al.* developed a database that lists all new STOP codons or loss of STOP codons, single-nucleotide variants, and short insertions and deletions. Mousepost.de compares these protein-inactivating mutations to the C57BL/6J background. Researchers can now easily search for naturally defective alleles in their strain of choice to determine whether these alleles impact the phenotype they are studying.

Timmermans, S. *et al. Proc. Nat. Acad. Sci. USA* **114**, 9158–9163 (2017).

CELL BIOLOGY

Optimized light-dependent dimerization

Optogenetic tools for controlling protein dimerization have become invaluable for probing cellular activities and pathways. Zhang *et al.* introduce two variants of the previously developed dimerizer NTH that offer improved features, such as increased light sensitivity and reversibility. NTH and its derivatives, CTH and TNH, are composed of three modules: *Escherichia coli* dihydrofolate reductase (eDHFR), a photocaged form of the eDHFR ligand trimethoprim fused to the Halo ligand, and the Halo-tag protein. In the presence of light, the ligand is uncaged, and this brings the eDHFR and the Halo-tag protein (and any proteins to which they are fused) together. The authors showcase the improved dimerizers by using them to study kinetochore function, showing that the molecular motor CENP-E is involved in directional chromosome transport and maintenance of metaphase alignment.

Zhang, H. *et al. Nat. Chem. Biol.* http://dx.doi.org/10.1038/nchembio.2456 (2017).

NEUROSCIENCE

Mechanistic insight into chemogenetics

Chemogenetic manipulation of neural activity is an alternative to optogenetics, especially for manipulations at longer timescales. In this technology, CNO (clozapine N-oxide) is thought to act on DREADDs (designer receptors exclusively activated by designer drugs) to induce a G-protein signaling cascade. However, Gomez *et al.* now show that CNO does not bind to DREADDs in cell culture or in brain slices. Instead, clozapine exhibits high affinity for DREADDs. Furthermore, the researchers find that, unlike clozapine, CNO does not cross the blood–brain barrier in mice. As CNO is known to convert to clozapine *in vivo*, the researchers propose that CNO, which has been widely used in chemogenetic experiments, acts on DREADDS via its clozapine metabolite. Indeed, they find that clozapine itself is more potent in mice than CNO is. Thus, they recommend using clozapine in chemogenetic applications.

Gomez, J.L. *et al. Science* **357**, 503–507 (2017).