TOOLS IN BRIEF

GENOMICS

A Cas9 knock-in mouse

The clustered, regularly interspaced, short palindromic repeats (CRISPR)-Cas9 system—which allows easy targeting of the Cas9 nuclease via a short guide RNA—has seen many applications in modifying the genomes of differentiated cell lines and embryonic stem cells, but its application to alter the genome of somatic cells *in vivo* is still limited. Platt *et al.* now introduce an inducible expression cassette for the Cas9 nuclease into the *Rosa26* locus in the mouse genome, generating a versatile tool for introducing mutations in any tissue of choice. The team achieved *ex vivo* genome editing in primary immune cells, *in vivo* targeted knockout of a neuron-specific gene and *in vivo* modeling of various cancer mutations, underscoring the utility of the Cas9 mouse for modeling disease.

Platt, R.J. *et al. Cell* **159**, 440–455 (2014).

BIOINFORMATICS

Getting a read on structural variation in cancer

Tumor genomes can have high structural variation caused by, for example, deletions, insertions and translocations. Detecting these variants in sequence data is challenging, and most tools specialize in finding certain mutation classes. Moncunill *et al.* take an unusual approach in their somatic mutation finder (SMUFIN), which compares tumor and matched normal genomic sequence reads directly and uses a tree structure to identify tumor-specific reads that are likely to bear mutations. Tumor reads are then grouped into blocks and processed by mutation type. SMUFIN can uncover single-base changes as well as structural variation of any size at base-pair resolution and does not rely on sequence alignment to a reference genome, making it fast. The researchers used SMUFIN to detect changes in blood and solid tumors, including highly complex variation indicative of chromothripsis.

Moncunill, V. *et al. Nat. Biotechnol.* doi:10.1038/nbt.3027 (26 October 2014).

SENSORS AND PROBES

Activity-based RNA probes

With recent studies showing that most RNAs are noncoding but functional, methods to study such RNAs are in high demand. McDonald *et al.* report a set of activity-based probes to enrich and identify bioactive RNAs. Reasoning that many bioactive RNAs have nucleophilic activity, the researchers screened for small-molecule electrophiles that would covalently modify only nucleophilic RNAs and not random RNA sequences. They synthesized their most promising probes in a biotinylated form to enable streptavidin-based affinity capture of bioactive RNAs. They then incubated their cocktail of eight activity-based probes with RNA fragments from nine different organisms and used selection and sequencing to identify reactive RNAs. This led them to discover a catalytic RNA from the archaebacterium *Aeropyrum pernix*, which shows promise as a tool for selectively labeling RNA with small-molecule tags.

McDonald, R.I. *et al. Nat. Chem. Biol.* doi:10.1038/nchembio.1655 (12 October 2014).

IMAGING

Sunny prospects for imaging and gene expression

The ability to amplify signals can be useful in a variety of biological contexts, such as in increasing transcription or improving fluorescence imaging. Tanenbaum *et al.* developed a protein tag that achieves such amplification. Their SunTag consists of up to 24 copies of a GCN4-derived peptide that bind multiple copies of specific single-chain antibodies. These antibodies can be fused to GFP for protein imaging purposes or to a Cas9 transcriptional activator for transcriptional applications. As the SunTag recruits up to 24 copies of GFP or Cas9, strong fluorescence or high transcriptional activity can be obtained. The researchers demonstrated this signal amplification in single-molecule imaging of motor, cytoplasmic, membrane-bound and mitochondria-associated proteins as well as for activating the overexpression of a chemokine receptor.

Tanenbaum, M.E. *et al. Cell* **159**, 635–646 (2014).

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