TOOLS IN BRIEF

CHEMICAL BIOLOGY

A method for labeling methionines

A plethora of methods are available for labeling cysteine residues in proteins. Methods for labeling that other sulfur-containing amino acid, methionine, have been challenging to develop owing to its weakly nucleophilic nature. Lin *et al.* report an approach for selective, rapid and robust labeling of methionine using oxaziridine-based reagents. Importantly, the reaction proceeds under biocompatible conditions. They illustrate several applications, including the addition of various tags to model proteins and the construction of antibody–drug conjugates. Moreover, they show that their chemoselective methionine-labeling approach can be used in combination with mass spectrometry to identify hyper-reactive methionine residues on a global proteome scale. The approach, named ReACT (redox-activated chemical tagging), should be a useful addition to the protein-labeling toolbox.
Lin, S. *et al. Science* **355**, 597–602 (2017).

GENE EXPRESSION

One mouse to trap them all

Broadly speaking, the epigenome regulates the transcriptome, and it is therefore desirable to profile chromatin states together with expression data. Doing so in pooled cells obscures cellular heterogeneity, and single-cell data derived from cultured cells may poorly reflect their *in vivo* counterparts. To isolate mRNA and nuclei from a desired cell type *in vivo*, Roh *et al*. developed a transgenic mouse line they call NuTRAP. It combines the TRAP (translating ribosome affinity purification) strategy—isolation of ribosome-bound mRNA from a cell type that expresses a GFP-tagged ribosomal protein—with nuclear tagging by a labeled nuclear membrane protein. The trapping cassette is activated by Cre-dependent removal of a STOP cassette. By breeding a NuTRAP mouse with a mouse expressing Cre only in adipocytes, the researchers were able to discover substantial differences in gene expression and epigenetic states between adipocytes *in vivo* and *in vitro*.
Roh, H.C. *et al*. *Cell Rep*. **18**, 1048–1061 (2017).

GENOMICS

Single-base editing

The capabilities of the Cas9 nuclease can be tuned by the effector it is fused to. Nuclease active or inactive versions of Cas9 have been harnessed to transcriptional activators or repressors, to enzymes that modify epigenomic marks and, most recently, to a cytidine deaminase that changes cytidines to uridines and hence converts C:G base pairs to T:A. The base editors are elegant but have nonetheless faced several limitations: the strict PAM requirement of *Streptococcus pyogenes* and a five-base-pair editing window within which all cytosines are modified. Kim *et al.* make base editing more versatile by using Cas9 variants with different PAM specificities and by narrowing the editing window to one or two base pairs by introducing mutations into the deaminase that affect its binding to DNA.
Kim, Y.B. *et al. Nat. Biotechnol.* http://dx.doi.org/10.1038/nbt.3803 (2017).

BIOINFORMATICS

Genome scaffolding while you sequence

As nanopore-based sequencing technology develops and matures, researchers are looking for creative ways to take advantage of its features, which include very long sequence reads and base-calling in near-real time. Cao *et al*. have designed the npScarf software, which uses long reads as a scaffold for fragmented genome assemblies generated from short reads. It uses the real-time base-calling feature in combination with rapid computation to determine when a sufficient level of scaffolding has been achieved, so that the sequencing run can be stopped to save further sequencing and computational resources. The approach performs well against other 'hybrid' long-read scaffolders that are used to improve the quality of short-read assemblies but lack real-time capabilities.
Cao, M.D. *et al*. *Nat. Commun*. **8**, 14515 (2017).