METHODS IN BRIEF

EPIGENETICS

Epigenome editing

Conclusions about the regulatory function of epigenetic marks such as histone methylation and acetylation are largely based on statistical association with gene expression; deciphering the role an individual mark plays in gene regulation is more challenging. Two recent reports tackle the targeted modification of histones at specific loci using the clustered, regularly interspaced, short palindromic repeats (CRISPR) system. Kearns *et al*. inactivate enhancers with a histone demethylase fused to nuclease-dead Cas9 (dCas9), and Hilton *et al*. target loci with an acetyltransferase-dCas9 fusion in order to regulate promoters and enhancers by activating transcription. Both approaches will allow a detailed understanding of the interplay between epigenetic modifications and gene expression.

Hilton, I.B. *et al. Nat. Biotechnol.* **33**, 510–517 (2015).
Kearns, N.A. *et al. Nat. Methods* **12**, 401–403 (2015).

CHEMICAL BIOLOGY

Chemical modification of native proteins

There exists a continuing need for novel approaches to chemically modify proteins at specific sites for applications in various research fields. Most methods require some amount of genetic engineering. MacDonald *et al.* present new chemistry for modifying native protein N termini that does not require any genetic engineering and that proceeds under mild conditions. They show that N-terminal amines react specifically and efficiently with a 2-pyridinecarboxyaldehyde to form a stable imidazolidinone product and that protein function is not adversely affected. They demonstrated the reaction for 12 diverse proteins, showing that it should be useful under many circumstances, such as for tagging proteins with biotin, fluorescent dyes, targeting moieties or affinity tags, to name just a few applications.

MacDonald, J.I. *et al. Nat. Chem. Biol.* **11**, 326–331 (2015).

GENE EXPRESSION

Transcripts in space

Single-cell RNA-seq allows tissues to be deconstructed into their component parts. Two new methods set out to 'reconstruct' tissues by projecting profiled cell types back onto the organismal map, leveraging spatial information for a small set of landmark genes from RNA *in situ* hybridization data. Satija *et al*. generate a discretized map of landmark gene expression and develop the computational tool Seurat, which cleans up RNA-seq signal on the basis of gene coexpression and assigns cells to the discretized map according to a statistical model of landmark gene expression. They sequence zebrafish blastula cells and map even rare cell types. Achim *et al*. offer a complementary approach that requires *in situ* data for only a small number of highly expressed genes to map single cells on the basis of RNA-seq data. The authors use the method to map cells from the brain of a marine annelid.

Achim, K. *et al. Nat. Biotechnol.* **33**, 503–509 (2015).
Satija, R. *et al. Nat. Biotechnol.* **33**, 495–502 (2015).

GENOMICS

Engineering the mosquito genome

The mosquito *Aedes aegypti* is the primary vector for pathogens that cause the potentially fatal illnesses chikungunya and yellow fever. Unlike the genomes of model organisms, the *A. aegypti* genome is incompletely mapped, making it challenging to engineer. Kistler *et al*. explore the use of clustered, regularly interspaced, short palindromic repeats (CRISPR) in the mosquito, with the ultimate goal of deciphering the genetic bases for chemosensory behavior in the insects—how female mosquitoes use odor cues to locate a host. The researchers injected embryos with Cas9 and guide RNA and observed deletions as well as insertions of a reporter construct via homology-directed repair. The mutations, which were transmitted to the germ line, offer a strategy for controlling vector populations.

Kistler, K.E. *et al. Cell Rep.* **11**, 51–60 (2015).