TOOLS IN BRIEF

IMAGING

Peptide-tag-specific nanobody for dSTORM

dSTORM is a super-resolution microscopy technique that offers nano-scale resolution for imaging of cellular structures. For dSTORM to achieve its full potential, the target of interest has to be labeled with fluorescent molecules at a high density. However, this often affects the assembly and function of the target protein. In addition, the size of conventional antibodies limits the achievable resolution of dSTORM. To address these issues, Virant *et al.* fused proteins of interest to a small peptide tag (BC2 tag) that does not interfere with normal protein function. For imaging, a high-affinity fluorescent nanobody (bivBC2-Nb) is applied that detects the protein tag. This tool also works in live cells and allows high-density labeling with minimal linkage errors and without disturbing protein function.

Virant, D. *et al. Nat. Commun.* **9**, 930 (2018).

GENOMICS

Off-targets in epigenome editing

Everybody agrees that DNA methylation has important regulatory roles, but many blanks regarding the details of this regulation remain to be filled in. The advent of CRISPR brought the promise of targeted modification of cytosines by fusing a methyltransferase to dCas9 and directing it to a locus of interest via guide RNAs (gRNAs). Galonska *et al.* examined this promise in a mouse embryonic stem cell line devoid of any DNA methylation and observed unexpectedly high background methylation, independent of gRNAs. The researchers replicated this finding in two somatic human cell lines; although they saw on-target activity at loci with low endogenous methylation, they also observed high genome-wide off-target activity. dCas9 fused to epigenetic effector proteins is a valuable tool, but more work is needed to ensure specificity.

Galonska, C. *et al. Nat. Commun.* **9**, 597 (2018).

STRUCTURAL BIOLOGY

Local resolution of cryo-EM maps with MonoRes

Resolution is perhaps the most important parameter for judging the quality of an electron density map determined by cryo-EM. The Fourier shell correlation (FSC) is the most common metric for estimating global resolution, but this approach cannot account for variance in the local resolution of different areas of the cryo-EM map. ResMap is the current state-of-the-art tool for estimating local resolution; although powerful, the method has several limitations. Vilas *et al.* address these limitations with their new tool MonoRes. An appealing and unique feature of MonoRes is that it produces a 3D resolution map; it is also fast and fully automated. The authors benchmarked its performance on both simulated and experimental cryo-EM maps, in comparison with ResMap and other tools. MonoRes is available via the Xmipp and Scipion software packages.

Vilas, J.L. *et al. Structure* **26**, 337–344 (2018).

GENOMICS

Genome editing with ease

Genetic manipulations in mice have become easier with the CRISPR-Cas9 system; however, the delivery of the necessary components into embryos, as well as the embryo handling, remains challenging. Yoon *et al.* now show that nucleic acid delivery methods such as microinjection and electroporation can be replaced by transduction of pre-implantation embryos with recombinant adeno-associated viruses (rAAVs). Many AAV serotypes can successfully transduce embryos, but serotype 6 proved to be the most efficient. When targeting the tyrosinase gene (involved in eye pigmentation and coat color), the researchers obtained chimeras with up to 100% efficiency, with most of the animals in the experiment developing into albinos. The researchers further simplified the genome-editing process in mice by introducing the rAAVs into oviducts of pregnant females, where embryos could be transduced *in situ*. Thus, this approach makes genome editing possible within pregnant animals, which avoids the need for embryo handling outside of the female reproductive tract.

Yoon, Y. *et al. Nat. Commun.* **9**, 412 (2018).