METHODS IN BRIEF

GENOMICS

CHAMP quantifies DNA-protein binding

Recycling has many benefits, as Jung *et al.* demonstrate on a repurposed MiSeq next-generation sequencing chip with 20 million spatially registered, unique DNA sequence clusters. On their chip-hybridized association-mapping platform (CHAMP), the DNA is labeled with a fluorescent maker and overlaid with fluorescent proteins. The researchers then record fluorescent intensity at each DNA cluster using a total internal reflection microscope. Computational analysis tells them which proteins bind to which DNA sequences. They apply CHAMP to a type-I CRISPR–Cas effector complex and show that this Cascade complex binds a six-nucleotide PAM. CHAMP also allows them to characterize off-target binding and develop a biophysical model for Cascade–DNA interactions.

Jung, C. *et al.* Cell **170**, 35–47 (2017).

NEUROSCIENCE

FAST imaging of whole brains

Several approaches for imaging of fluorescently labeled whole brains are available, but they suffer from either slow speed or low resolution. Seiriki *et al.* have sped up the process of imaging in their block-FAce Serial microscopy Tomography (FAST) approach. They combine a spinning-disk-based confocal microscope with a tissue microslicer. With their setup, they acquire tiled image stacks, shave off the imaged brain slice, and then repeat the imaging and slicing until the whole brain is imaged. The approach is fast enough to image whole mouse brains at subcellular resolution in less than three hours. Furthermore, it is possible to collect the brain slices in order to conduct *post hoc* immunohistological analyses. The researchers have also scaled up the approach to marmoset and human post-mortem brains.

Seiriki, K. *et al. Neuron* **94**, 1085–1100 (2017).

EPIGENETICS

Chromosome accessibility and methylation status in one

Nucleosome occupancy and methylome sequencing (NOMe-seq) relies on a special methyltransferase to methylate cytosines in enzyme-accessible GpC dinucleotides. Subsequent bisulfite sequencing reveals methylated GpCs, which correspond to nucleosome-free regions (associated with active gene regulation), as well as endogenous DNA methylation at CpG dinucleotides, which constitutes a regulatory epigenetic mark. Pott has adapted NOMe-seq for low input and has shown that the approach can be used to measure these chromatin features in single nuclei. He recovered accessibility and DNA methylation patterns in single cells from human lymphoblastoid cell lines at genomic sites designated as accessible by DNase hypersensitivity assays in bulk cell samples. Pott also leveraged the high density of GpCs in the genome to identify putative transcription-factor-binding footprints in the accessibility data. Single-cell NOMe-seq will help researchers to unravel epigenetic heterogeneity in complex samples.

Pott, S. *eLife* **6**, e23203 (2017).

GENETICS

Limits of gene drives

Super-Mendelian inheritance, during which one allele of a heterozygous locus is passed down to the majority of offspring, has a number of interesting applications such as controlling the fertility of disease vectors. Such gene drives are relatively easy to design with the CRISPR system that cuts the undesirable allele followed by homology-driven repair to replace it with the allele of choice. However, resistance alleles, no longer cut by Cas9, also develop rapidly. Champer *et al.* now quantify the rate of resistance-allele formation in flies using two gene drives to replace the X-linked *yellow* gene with a fluorescent protein. From the high percentage of resistance alleles in germline cells and embryos, the researchers conclude that new designs are needed if a gene drive is to spread in a wild population.

Champer, J. *et al. PloS Genet.* http://dx.doi.org/10.1371/journal.pgen.1006796 (2017).