**Editing the malaria parasite genome**

Engineered zinc-finger nucleases (ZFNs) have been used to edit the genomes of many species. The double-strand break generated by a ZFN is typically resolved either by nonhomologous end joining (NHEJ), an error-prone process that can result in small insertions or deletions leading to gene disruption, or by homology-directed repair in the presence of a donor sequence. Fidock and colleagues now report methods for genome editing in the malaria parasite *Plasmodium falciparum*. This organism lacks components of the NHEJ pathway and is expected to repair DNA breaks via homologous recombination. Delivering both members of a ZFN pair as well as the donor template on a single plasmid, the authors demonstrate complete gene replacement of an integrated reporter as well as more precise gene editing of an endogenous gene, both with and without selection.

*Article p993*

**Bringing order to chromatin interaction maps**

When it comes to DNA, it is not just about the sequence, it is also about interaction—who talks to whom? Various iterations of chromatin conformation capture methods have provided insight into this question, but their output is not easy to interpret, making the creation of unbiased, high-resolution maps difficult. Mirny, Dekker and colleagues describe a pipeline to normalize Hi-C data (which provides an all-against-all comparison of DNA interaction sites) that removes bias from contact probabilities and gives new insight into chromatin organization. de Laat, Tanay and colleagues improve the analysis of 4C data (which reports the interaction between a single site and the rest of the genome) to achieve higher resolution.

*Brief Communication p969, Article p999, News and Views p961*

**Reversible protein labeling**

An ideal protein tag enables many applications, such as imaging or purification, and can be removed or exchanged at will. Burkart and colleagues generate such a reversible label using an acyl carrier protein (ACP). ACP—which occurs naturally and plays a role in lipid biosynthesis but can easily be fused to any protein of interest—is post-translationally modified by a phosphopantetheine, which in turn can be conjugated to any tag of choice. Using an ACP hydrolase and a phosphopantetheinyl transferase, Burkart and colleagues showed that the PPant conjugate can be removed or swapped for a different one, allowing the iterative labeling of ACP or ACP fusion proteins. This rapid and reversible modification provides flexibility for studies that seek to apply different tags for different purposes to the same protein.

*Brief Communication p981*

**Exonucleases for better gene disruption**

The propensity of the NHEJ pathway to introduce small insertions and deletions during the repair of an endonuclease-mediated DNA double-strand break (DSB) is increasingly exploited to carry out precise gene disruption. However, the DSB can be precisely repaired and re-cleaved several times before mutation destroys the target site. Scharenberg, Rawlings and colleagues demonstrate that DNA exonucleases delivered concomitantly with a targeted endonuclease can improve the frequency of gene disruption, presumably by limiting the number of precise repair events. By systematically screening a panel of DNA end–processing enzymes with all three targeted endonuclease platforms, they identify exonucleases—in particular, TRex2—that improve the disruption frequency of integrated reporters and of endogenous genes in mammalian cells.

*Brief Communication p973*

**Worm screens on autopilot**

Many graduate student and postdoc hours have been spent carefully imaging, analyzing and classifying—one by one—the thousands of worms that result from forward genetic screens. Whole-organism screens have not been as amenable to automation as their cellular counterparts, particularly when searching for subtle morphometric phenotypes and hard-to-see structures like synapses. Lu and colleagues now offer an alternative to the painstaking process of manual worm screening through an integrated system composed of a microfluidic device, computer-vision tools and statistical methods. Their setup can handle live worms automatically, imagining them at high resolution, classifying and sorting them. To prove the capabilities of the system, they put it to work for the detection of mutants involved in synaptogenesis.

*Brief Communication p977*