IN BRIEF

⮕ MODEL ORGANISMS

Systematic mouse-mutant characterization

International efforts are underway to knock out every mouse gene and carry out comprehensive phenotyping on the resulting lines. As a step towards this goal, the authors carried out viability and fertility screening of 489 mutant lines and systematically screened for adult phenotypes in 250 of these lines. Demonstrating the importance of this approach, they describe phenotypes for many previously unpublished genes and also find many phenotypes that would not have been uncovered without systematic screening. Their findings also revealed unexpectedly high levels of haploinsufficiency and pleiotropy.

ORIGINAL RESEARCH PAPER White, J. K. *et al.* Genome-wide generation and systematic phenotyping of knockout mice reveals new roles for many genes. *Cell* **154**, 452–464 (2013)

⮕ EPIGENETICS

Understanding resistance to cancer drugs

DNA hypomethylating agents such as decitabine are used to treat myeloid cancers and are thought to work by reactivating tumour suppressor genes that have been silenced by DNA methylation. However, cancers become resistant to these drugs, and this may be due to gene re-silencing. These authors provide evidence that re-expression of the *MLH1* tumour suppressor gene in colon cancer cells following decitabine treatment involves both DNA demethylation and nucleosome eviction at promoters. Importantly, after decitabine withdrawal, the initial step in re-silencing is nucleosome reassembly, which occurs before remethylation — a finding with implications for combatting drug resistance.

ORIGINAL RESEARCH PAPER Hesson, L. B. *et al.* Reassembly of nucleosomes at the *MLH1* promoter initiates resilencing following decitabine exposure. *PLoS Genet.* http://dx.doi.org/10.1371/journal.pgen.1003636 (2013)

⮕ HUMAN GENETICS

Local ancestry inference gets faster and better

In many populations, ancestry varies at different genomic regions; the ability to infer local ancestry is important for applications ranging from personalized medicine to studying the history of human populations. However, current computational methods for local ancestry inference are slow and can only detect ancestry at the continental level. This study presents a new and faster approach, which infers ancestry at a finer level: the authors used it to show that African Americans have low levels of Native American ancestry.

ORIGINAL RESEARCH PAPER Maples, B. K. *et al.* RFMix: a discriminative modeling approach for rapid and robust local ancestry inference. *Am. J. Hum. Genet.* http://dx.doi.org/10.1016/j.ajhg.2013.06.020 (2013)

⮕ TECHNOLOGY

CRISPR tool for regulating gene expression

This study presents a method for specific, stable and efficient regulation of eukaryotic genes. The prokaryotic CRISPR system provides adaptive immunity by RNA-guided targeting of CRISPR-associated (Cas) proteins to specific genomic sites. It has already been adapted for use in eukaryotic genome editing. This study now shows that a Cas protein can be fused to different regulatory domains to either activate or repress the transcription of target genes in eukaryotes, guided by a co-expressed short RNA. The simplicity of the system should make it fast and cheap to produce tools to target many genes of interest.

ORIGINAL RESEARCH PAPER Gilbert, L. A. *et al.* CRISPR-mediated modular RNA-guided regulation of transcription in eukaryotes. *Cell* **154**, 442–451 (2013)