IN BRIEF

TECHNOLOGY

Tracking genome engineering outcome at individual DNA breakpoints

Certo, M. T. *et al. Nature Methods* **8**, 671–676 (2011)

Genome editing using engineered nucleases requires homology-directed DNA repair (HDR) to insert a donor cassette at the targeted dsDNA break, rather than repair by non-homologous end joining (NHEJ). Certo *et al.* developed a fluorescent reporter system to distinguish between these outcomes. Working in human cells, they showed that HDR is favoured by a high concentration of donor template, by ssDNA (rather than dsDNA) breaks and by suppression of the NHEJ factor DNA-dependent protein kinase (DNA-PK).

EPIGENETICS

Tet proteins can convert 5-methylcytosine to 5-formylcytosine and 5-carboxylcytosine

Ito, S. *et al. Science* 21 Jul 2011 (doi:10.1126/science.1210597)

Tet-mediated formation of 5-carboxylcytosine and its excision by TDG in mammalian DNA

He, Y. F. *et al. Science* 4 Aug 2011 (doi:10.1126/science.1210944)

Two reports reveal that TET family protein activity, as well as hydroxylating 5-methylcytosine (5mC) in DNA to 5-hydroxymethylcytosine (5hmC), results in the formation of 5-formylcytosine (5fC) and 5-carboxylcytosine (5caC). He *et al.* showed that 5caC is an intermediate that allows the 5hmC mark to be removed by base excision, and Ito *et al.* demonstrated the wide prevalence of 5fC and 5caC in mouse embryonic stem cells and tissues.

GENE REGULATION

Discovering transcription factor binding sites in highly repetitive regions of genomes with multi-read analysis of ChIP–seq data

Chung, D., *et al. PLoS Comp. Biol.* **7**, e1002111 (2011)

A version of ChIP–seq that uses reads that map to multiple regions of a reference genome rather than to a unique location proves useful for identifying transcription factor binding sites in repetitive genomic regions. When this approach was applied to human STAT1 and mouse GATA1 ChIP–seq data sets, it detected new peaks in segmentally duplicated regions, in which signals are difficult to map, and improved peak detection in mappable regions.

STEM CELLS

Generation of healthy mice from gene-corrected disease-specific induced pluripotent stem cells

Wu, G. *et al. PLoS Biol.* **9**, e1001099 (2011)

These authors corrected a genetic defect in induced pluripotent stem cells (iPSCs) from a mouse disease model and used the repaired cells to generate gene-corrected mice. Wu *et al.* derived iPSCs from mice with fumarylacetoacetate hydrolase (FAH) deficiency. They used these iPSCs to generate mutant *Fah*$^{-/-}$ mice, showing that *Fah*$^{-/-}$ iPSCs were pluripotent. The mutant iPSCs were gene-corrected using a lentiviral vector and were successfully used to make healthy, genetically rescued mice — the first time that gene-corrected iPSCs have been reported to maintain a fully pluripotent phenotype.