TOOLS IN BRIEF

EPIGENETICS

A growing toolbox to study the epigenome

Methylation of DNA at cytosine bases is an important mechanism to regulate gene expression, but studying the functional role of this epigenetic change requires specific methods to demethylate CpGs in a targeted manner in the genome. Maeder *et al.* describe an approach for demethylating cytosine that involves fusing the human TET1 hydroxylase catalytic domain to engineered transcription activator–like effector (TALE) repeats. This framework can be programmed to target essentially any DNA sequence using the TALE repeat code, and it allowed the authors to induce locus-specific demethylation at three endogenous genes in three different human cell lines and study the effects on gene expression. The authors found that the efficiency of the process depended on the genomic locus that was targeted. Control experiments accounted for off-target and nonspecific effects. The method provides researchers with a useful tool for studying the functional significance of epigenetic events.

Maeder, M.L. *et al. Nat. Biotechnol.* doi:10.1038/nbt.2726 (9 October 2013).

CHEMISTRY

Light-guiding hydrogels

Hydrogel polymers have properties well suited for cell encapsulation and are increasingly being used for cell transplantation experiments in animal models. Tailoring hydrogels so that their light-transmission capabilities can be exploited adds new functionality. As shown by Choi *et al.*, modifications of the shape and structure of poly(ethylene glycol)-based hydrogels can improve their light-guiding properties. The authors found that longer polymers yielded a higher transparency after cross-linking. They implanted patches of hydrogels containing cells in awake, freely moving mice for several days to characterize the long-term transparency, biocompatibility, cell viability and light-guiding properties. They then used these light-guiding hydrogels for optogenetic stimulation of glucagon-like peptide 1–secreting cells in a mouse model of diabetes and for real-time *in vivo* readouts of quantum-dot toxicity in reporter cells.

Choi, M. *et al. Nat. Photonics* doi:10.1038/nphoton.2013.278 (20 October 2013).

BIOINFORMATICS

Gene expression UPCs

To get the most out of the vast collection of public gene expression data, one should be able to compare values in any data set. But different data generation methods introduce unique biases, making it possible to assess only relative expression within a platform. Gene expression barcodes have been used to estimate absolute expression from microarray data by normalizing values against a large reference expression data set. Piccolo *et al.* extend this idea with their universal expression code (UPC) algorithm, which models noise according to genomic base composition and target-region length and estimates transcriptional activity using a mixture model. UPC values range from 0 to 1 and can be directly compared across microarray and RNA sequencing platforms. The method does not need a large reference panel, and new data sets can be added incrementally.

Piccolo, S.R. *et al. Proc. Natl. Acad. Sci. USA* **110**, 17778–17783 (2013).

STEM CELLS

Towards stem cell–derived human blood

Human pluripotent stem cells (hPSCs) can be differentiated along the blood lineage, but long-term repopulation of hematopoietic stem cells with multilineage differentiation potential remains elusive. Doulatov *et al.* describe a promising strategy to achieve this goal. Starting with hPSC-derived hematopoietic progenitors, they screened a set of known transcriptional regulators and identified three—HOXA9, ERG and RORA—that promoted self-renewal and increased the differentiation potential of the cells *in vitro*. Two additional factors, SOX4 and MYB, yielded hPSC-derived cells with short-term engraftment potential and with myeloid and erythroid lineage potential *in vivo*. Further factors may in the future reconstitute more complete blood stem cell function in hPSC-derived cells, enabling a broadened scope for their application in disease modeling and drug screening.

Doulatov, S. *et al. Cell Stem Cell* **13**, 459–470 (2013).