TOOLS IN BRIEF

BIOINFORMATICS

Computing single-cell trajectories

Following gene expression over time is critical to understanding dynamic cellular processes such as differentiation, and collecting data from single cells has the potential to untangle these phenomena at high resolution. Trapnell *et al.* introduce Monocle, an unsupervised algorithm that can place single cells in 'pseudotemporal' order on the basis of their expression profiles. The researchers used Monocle to investigate the differentiation of myoblast progenitors into muscle. They were able to identify key events in differentiation that were not detected by bulk cell sequencing or single-cell profiles ordered by time of collection. Monocle also detected alternate differentiation trajectories and a group of undifferentiated cells. The increased temporal resolution allowed the researchers to perform better gene coexpression analysis and identify eight new transcription factors implicated in muscle development.

Trapnell, C. *et al. Nat. Biotechnol.* **32**, 381–386 (2014).

MODEL ORGANISMS

Monkey mutants with TALENs

Models of human disease in nonhuman primates are of high interest in biomedicine, and targeted genome-editing technologies offer a way to realize this goal. In recent work, Liu *et al.* demonstrated the use of transcription activator–like effector nucleases (TALENs) to mutate the *MECP2* gene in rhesus and cynomolgus macaques and thus to generate a primate model of Rett syndrome, an X-linked neurodevelopmental disease. The researchers used three TALEN pairs targeting the gene at different positions and delivered the nucleases to one-cell zygotes as plasmid DNA. They were able to efficiently modify the gene in embryos and did not detect any off-target effects. After implantation, male fetuses carrying *MECP2* mutations were miscarried, as in humans. Female mutant monkeys were carried to term and, at the time of publication, had not yet presented a phenotype.

Liu, H. *et al. Cell Stem Cell* **14**, 323–328 (2014).

SENSORS AND PROBES

Microbially produced ultrasound reporters

Though ultrasound technology has been used in research and medicine for decades, it is rarely used for molecular imaging owing to a lack of suitable nanoscale reporters. Conventional ultrasound contrast agents include gas microbubbles surrounded by a lipid or protein shell, but these reporters have several limitations, including poor stability. Shapiro *et al.* recently harnessed microbially produced gas vesicles, which are nanoscale compartments filled with gas and surrounded with a protein shell and are used by the organisms for buoyancy control in aquatic environments. The researchers purified the gas vesicles from the microbes and used them as ultrasound contrast agents, finding that they had high stability and were suitable for *in vivo* molecular imaging in mice. Further work is needed to ensure control over size and shape and to optimize circulation time and biocompatibility.

Shapiro, M.G. *et al. Nat. Nanotechnol.* **9**, 311–316 (2014).

STEM CELLS

A small-molecule label for stem cells

Probes for detecting human pluripotent stem cells (hPSCs) are needed for basic research and therapeutic applications. Hirata *et al.* performed a screen of a fluorescent small-molecule library and identified a rhodamine derivative, KP-1, that shows promise as a label for hPSCs in some contexts. Labeling with KP-1 appears to be due to the fact that hSPCs inhibit the expression of ABC drug transporters ABCB1 and ABCG2, which export KP-1 from other cells. Labeling with KP-1 is not entirely specific: the probe shows only weak labeling of hematopoietic stem cells, hPSC-derived cardiomyocytes and several other human cell types, but it strongly labels neural stem cells, astrocytes and some cancer cell lines. The researchers also determined that KP-1 probably cannot be used to identify fully reprogrammed cells during the induction of pluripotency.

Hirata, N. *et al. Cell Rep.* **6**, 1165–1174 (2014).