# METHODS IN BRIEF

STEM CELLS

## Chemically induced pluripotent stem cells

Reprogramming of somatic cells to induced pluripotency has thus far been achieved by the forced expression of one or more transcription factors. Hou *et al.* have now identified conditions in which mouse somatic cells of embryonic, neonatal and adult origin can be reprogrammed to pluripotency using small molecules alone. The researchers identified an effective cocktail by screening chemical collections for molecules that could bypass the requirement for exogenous Oct4 both early and late in the reprogramming process. The resulting cells resemble embryonic stem cells and conventional induced pluripotent stem cells with respect to several molecular markers, and contribute to all germ layers of chimeric mice, including the germ line.

Hou, P. *et al. Science* doi:10.1126/science.1239278 (18 July 2013).

SYSTEMS BIOLOGY

## Protein complexes under perturbation

Examining protein-protein interactions (PPIs) is not in itself enough to understand cell organization and function. Rather, the way in which these networks change under perturbation must also be studied. A recent report outlines a strategy and resources for examining PPIs in varying genetic backgrounds in yeast. Diss *et al.* use a protein complementation assay of dihydrofolate reductase to systematically examine PPIs in selected yeast strains from a gene knockout collection. They used synthetic genetic array technology to assemble the strain collections needed for these studies and then systematically examined interactions in two protein complexes, the nonessential retromer and the essential nuclear pore complex, in multiple genetic backgrounds.

Diss, G. *et al. Cell Rep.* **3**, 2155–2167 (2013).

MICROSCOPY

## Real-time image processing

In multiview light-sheet microscopy, the use of several objectives enables one to image developing embryos over time and to obtain images from different views of the same region. But processing all these images offline requires massive storage and computing power. As an alternative, Schmid *et al.* develop a pipeline for processing and compressing images in real time, reducing the overall data that is stored. As a demonstration, they imaged zebrafish embryos that expressed GFP in endoderm cells using a multiview light-sheet microscopy setup. They approximated the shape of the embryo to a sphere and applied radial maximal intensity projections to produce two-dimensional images of the entire three-dimensional embryo. The resulting dataset requires gigabytes instead of terabytes for storage and enables visualization of cell migration patterns in entire embryos.

Schmid, B. *et al. Nat. Commun.* **4**, 2207 (2013).

IMAGING

## Imaging nascent proteins in living cells

A cell's proteome is highly dynamic in nature, reflecting the cell cycle and surrounding environment. Newly synthesized proteins can be visualized in the cell using fluorescence-based methods, but such approaches generally require fixation. Imaging mass spectrometry–based methods, though powerful, require destruction of the cell. Wei *et al.* now apply stimulated Raman scattering (SRS) microscopy to image nascent proteins in live mammalian cells without fixation or staining. The method is simple and results in minimal cell perturbation: nascent proteins incorporate deuterium-labeled leucine, which, based on its unique vibrational signature, can be readily detected by SRS microscopy. Application of the method highlighted rapid protein turnover in nucleoli (the sites of ribosome biogenesis) and in neurites of neuron-like cells during differentiation.

Wei, L. *et al. Proc. Natl. Acad. Sci. USA* **110**, 11226–11231 (2013).