**Mammalian genetic interaction mapping**

The knowledge of whether two genes interact—that is, whether the phenotype of a double mutant differs from the sum of the phenotypes from each individual mutation—has led to important insights in simple model organisms such as yeast, in which knocking out pairs of genes is feasible. Two independent groups now look at genetic interactions in mammalian cells on a large scale by applying RNAi strategies to reduce the expression of gene pairs. Krogan, Panning, Bandyopadhyay and colleagues use pairs of endonuclease-prepared small interfering RNAs (esiRNAs) to monitor fitness and map chromatin complexes in mouse fibroblasts. Boutros, Huber and colleagues map epigenetic regulators in human colon cancer cells with pairs of siRNAs and multiparametric phenotypic readouts.

*Articles p427, p432, News and Views p397*

**Light sheets for biological discovery**

The technique of illuminating a sample with a thin sheet of light from the side while recording emitted fluorescence from the top or bottom has proven of great value for biological imaging. Light-sheet microscopy offers—among other benefits—high imaging speeds, high-sensitivity detection and three-dimensional imaging with low phototoxicity and photobleaching. Two Articles published in this issue show the value of light-sheet imaging for biological discovery at different scales. Keller, Ahrens and colleagues use a high-speed light-sheet microscope to image the whole brain of a zebrafish larva every 1.3 s, recording the activity of neurons at the cellular level using the calcium indicator GCaMP5G. Xie and colleagues image the nuclei of living cells with single-molecule sensitivity. To do this, they developed a variant of the light-sheet setup in which the light sheet is generated by reflecting a laser beam incident from the top by a small mirror.

*Articles p413, p421*

**Zinc-finger barcodes**

Studying complex and heterogeneous cell populations requires methods to label and manipulate different subsets of cells. Mali, Church and colleagues apply programmable DNA-binding domains for this purpose. With zinc-finger domains expressed on the cell surface, cells can be labeled with a cognate, fluorescently tagged oligonucleotide and processed either by fluorescence imaging or flow cytometry. The approach is specific and extensible and can be used in a sequential quench-and-reprobe mode to detect a larger number of subpopulations than available fluorophores can detect. It can also be used to physically isolate cells or achieve targeted delivery to subsets of cells.

*Brief Communication p403, News and Views p399*

**mNeonGreen**

Much recent effort in fluorescent protein development has been focused on engineering red and far-red fluorescent proteins, in part because they are useful for *in vivo* imaging. But improvements in other regions of the spectrum are still welcome. Shaner and colleagues now describe mNeonGreen, one of the brightest green fluorescent proteins to date. Starting with the tetrameric yellow fluorescent protein LanYFP from *Branchiostoma lanceolatum*, the researchers used structural modeling to engineer a monomeric form of the protein. The resulting mNeonGreen can be successfully fused to several cellular proteins, is bright and photostable, and will be useful in fluorescence resonance energy transfer sensors and stochastic single-molecule super-resolution imaging as well as more standard imaging applications.

*Brief Communication p407*

**Adhesion-based stem cell purification**

Building on a systematic study of the adhesion properties of human pluripotent stem cells (hPSCs), García and colleagues describe a label-free approach to separate hPSCs from other cells in a culture. Both human embryonic and induced pluripotent stem cells differ from somatic cells or more differentiated cells by the strength with which they adhere to the culture substrate. Fluid flow-controlled shear force, applied in a microfluidic device, can thus be used to exploit this differential adhesion and to separate hPSCs from other cell types. García and colleagues use this approach to separate fully reprogrammed induced hPSCs from partially reprogrammed cells. The approach is a simple and label-free complement to isolation methods that require labeling the surface of cells.

*Article p438*