TOOLS IN BRIEF

SENSORS AND PROBES

Imaging when cells get together

If two proteins meet in a cell, chances are that the event can be captured by one of several methods to image protein interactions. But what about detecting two cells that get close in the body? Sellmyer *et al*. describe a cellular proximity assay based on bioluminescence. Glucose-caged luciferin (Lugal) is fed to cultured cells or to animals, and activator cells expressing β-galactosidase uncage it. The luciferin is then free to diffuse into the surrounding medium, where reporter cells expressing luciferase can take up the luciferin and emit detectable light. Close proximity between activators and reporters leads to brighter luminescence. This assay allowed the researchers to see populations of cells that greet each other in the Petri dish as well as immune cells that associate with breast cancer metastases in the mouse.

Sellmyer, M.A. *et al*. *Proc. Natl. Acad. Sci. USA* **110**, 8567–8572 (2013).

BIOINFORMATICS

Visualizing high-dimensional data

As technologies mature that can monitor many parameters simultaneously on single cells, visualization of the resulting data is becoming a bottleneck. One may be able to label heterogeneous cellular populations for tens of surface markers using mass cytometry, for instance, but methods to interpret the signals in terms of the underlying population structure are still limited. Amir *et al*. now report viSNE, a tool for the interpretation and visualization of high-dimensional data, in which single-cell resolution is maintained. The algorithm projects the data from high-dimensional to two-dimensional (2D) space; in the resulting 2D scatter plot, each point represents the position and relationships of a cell in high-dimensional space. Applied to normal human bone marrow, viSNE reproducibly returns expected cell subpopulations; leukemic bone marrow, by contrast, shows a comparatively abnormal structure.

Amir, E.-a.D. *et al*. *Nat. Biotechnol*. **31**, 545–552 (2013).

IMAGING

Hyperpolarized silicon particles for MRI

Biocompatible, background-free, inexpensive, readily available, and easily functionalizable silicon-based particles are attractive agents for a growing number of imaging technologies, including magnetic resonance imaging (MRI). Cassidy *et al*. show that silicon particles offer many favorable properties that prior MRI imaging agents have not. In particular, the ^{29}Si nuclei in silicon particles can be hyperpolarized (meaning polarization can be increased far beyond its equilibrium value), thereby greatly boosting their MRI signal. Cassidy *et al*. showed several *in vivo* applications to demonstrate the use of hyperpolarized silicon particles for MRI, including imaging mouse gastrointestinal tract, vena cava and prostate tumors. They also characterized properties crucial for potential clinical applications, observing no toxicity and finding that the particles were cleared within 2 weeks.

Cassidy, M.C. *et al*. *Nat. Nanotechnol*. **8**, 363–368 (2013).

IMMUNOLOGY

Active T cells on the run

The initial steps that lead to the activation of T cells during an immune response are currently of high interest. Two reports provide genetic tools for *in vivo* imaging of T-cell activation in rodents in real time. Because early activation events in lymphocytes involve changes in intracellular calcium levels, Mues *et al*. used a genetically encoded calcium indicator to label and then track T cells using two-photon microscopy. They found that the sensor, TN-XXL, which has been used for a range of studies in the nervous system, was not efficiently expressed in lymphocytes, so they optimized TN-XXL to improve its expression in T cells. In separate work, Lodygin *et al*. engineered a molecular sensor based on the protein nuclear factor of activated T cells and the histone protein H2B. The sensor labeled the initial and late phases of T-cell activation and could be used for intravital imaging of immune processes.

Lodygin, D. *et al*. *Nat. Med*. **19**, 784–790 (2013).

Mues, M. *et al*. *Nat. Med*. **19**, 778–783 (2013).