METHODS IN BRIEF

CHEMICAL BIOLOGY

Detecting kiss-and-run interactions with LIPSTIC

Many immune processes depend on brief 'kiss-and-run' interactions between different cell types, but detecting the involvement of specific receptors and ligands has been a challenge. Pasqual *et al.* present LIPSTIC (labeling immune partnerships by SorTagging intercellular contacts), a method that detects receptor–ligand interactions between cells, even in living mice. The approach relies on the harnessing of bacterial sortase A, which is fused to a receptor (or ligand) of interest. A tag containing a 5-glycine N-terminal motif is fused to the complementary ligand (or receptor). Sortase A transfers a biotinylated or fluorescently labeled substrate peptide to this 5-glycine motif, thereby installing it on the ligand. Using this approach, the authors found that CD40–CD40L interactions between dendritic cells and $CD4^+$ T cells occur at two different stages during T cell priming.

Pasqual, G. *et al. Nature* **553**, 496–500 (2018).

GENOMICS

Single-cell hat trick

In sports, a 'hat trick' is a feat accomplished three times in a row by the same player. Clark *et al.* have achieved their own hat trick of a sort, with the first method for extracting three types of genome-wide data from the same cell. Their single-cell nucleosome, methylation and transcription sequencing (scNMT-seq) method combines features of their previous single-cell methylation and transcriptome sequencing (scM&T-seq) approach and of nucleosome occupancy and methylation sequencing (NOMe-seq). The researchers separate RNA and DNA, sequence the RNA fraction and apply a GpC methyltransferase to the DNA prior to bisulfite sequencing. The externally supplied GpC mark labels enzyme-accessible, nucleosome-poor regions of the genome, and provides higher-coverage information than other DNA accessibility assays, and bisulfite conversion of methylated cytosines also allows traditional CpG DNA methylation to be inferred. The authors explore links between transcription and these two epigenetic features in differentiating mouse embryonic stem cells.

Clark, S.J. *et al. Nat. Commun.* **9**, 781 (2018).

NEUROSCIENCE

A clear window into the brain

Imaging neuronal structure or activity *in vivo* requires invasive window preparations because of the skull's opacity, but such approaches are technically demanding and associated with inflammation. Zhao *et al.* present an alternative method for obtaining a clear view of the mouse brain. The researchers found that application of either collagenase or the chelator EDTA (depending on the animal's age) followed by glycerol renders the mouse skull optically transparent. In mice up to one month old, the researchers could image neuronal morphology (including spines), microglia, vasculature and calcium activity through the cleared skull. For older animals, the technology could be combined with thinning of the skull for similar results. The method does not result in noticeable inflammation and can be repeated for longitudinal imaging studies.

Zhao, Y.-J. *et al. Light: Science & Application* **7**, 17153 (2018).

STEM CELLS

From somatic cells to naive pluripotent cells

Standard human pluripotent stem cells (hPSCs) appear to be equivalent in many ways to post-implantation epiblast-derived murine stem cells (so-called epi-SCs). A number of methods are now available to convert hPSCs to a 'naive' state in which they resemble pre-implantation mouse pluripotent stem cells, akin to a true developmental ground state. Kilens *et al.* developed a method for converting somatic cells directly to naive hPSCs, using overexpression of the four Yamanaka transcription factors (Oct4, Klf4, cMyc and Sox2) in an established 'T2iLGö' naive hPSC medium. The authors stress that to evaluate pluripotency, it is critical to carefully benchmark naive hPSCs against human pre-implantation epiblast cells at the level of the transcriptome, mitochondrial respiration and X-chromosome inactivation status.

Kilens, S. *et al. Nat. Commun.* **9**, 360 (2018).