METHODS IN BRIEF

NEUROSCIENCE

Hi-res spatial gene expression in the brain

In situ hybridization is a trusted method for obtaining high-resolution spatial expression patterns in organ slices, but the traditional one-gene-at-a-time approach is laborious and does not allow correlations to be drawn between multiple transcripts in the same cell. Shah *et al*. have improved their multiplexed sequential fluorescence *in situ* hybridization (SeqFISH) approach and applied it to study the mouse hippocampus. They used the temporal barcoding of five fluorophores to study 125 genes with a new, time-efficient correction scheme that minimizes false calls from erroneously imaged probes. The method incorporates the hybridization chain reaction to amplify signal for more robust detection. By imaging these genes simultaneously in nearly 15,000 cells in tissue sections, the researchers uncovered subregions within the hippocampal CA1 and CA3 regions that exhibit distinct transcriptional profiles.

Shah, S. *et al. Neuron* **92**, 342–357 (2016).

STEM CELLS

Man-made mouse eggs

The mature oocyte represents a critical resource for studying mammalian development as well as reproduction and fertility. Hikabe *et al*. now report a culture system for generating fertilization-competent mouse oocytes from fibroblast-derived pluripotent stem cells in about 30 days. The researchers previously showed that it is possible to differentiate mouse pluripotent stem cells into primordial germ-cell-like cells that can become functional oocytes. However, the transformation from germ cell to gamete required transplantation into adult female mice. In their new, fully *in vitro* method, primordial germ-cell-like cells are cocultured with female gonadal somatic cells, and hormones, inhibitors and other factors are administered at key stages to stimulate the development of a follicular environment and to coordinate stages of the egg cell's maturation.

Hikabe, O. *et al. Nature* http://dx.doi.org/10.1038/nature20104 (2016).

STRUCTURAL BIOLOGY

Laser ablation for growing protein crystals

The growth of large, high-quality protein crystals for X-ray diffraction studies is more of an art than a science, requiring extensive testing of different conditions. Tominaga *et al*. now show how crystal growth can be stimulated with light—more specifically, femtosecond laser ablation. They used femtosecond pulses of laser light to etch one side of a hen egg white lysozyme crystal, which caused disruptions to the crystal lattice. This disruption switched the mechanism of crystal growth from slow two-dimensional nucleation to faster spiral-growth mode. The method produced a hillock-shaped lysozyme crystal that was 30% larger than the original crystal, with quality similar to that of traditionally grown crystals. The approach may find use in traditional structural biology as well as in the materials field.

Tominaga, Y. *et al. Nat. Photon.* **10**, 723–726 (2016).

MOLECULAR BIOLOGY

Annotating RNAs by the company they keep

An RNA's sequence is a poor predictor of its function, particularly for noncoding RNAs, which come in many different lengths and structures. To improve annotation, Smirnov *et al*. profiled the association of RNA with RNA-binding proteins by Grad-seq (gradient profiling by sequencing). They first partitioned cell lysates from *Salmonella enterica* by glycerol gradient centrifugation to sort complexes by size and shape. Each fraction's RNA was then sequenced and proteins were analyzed by liquid chromatography–tandem mass spectrometry. Clustering by principal-component analysis revealed two major branches: coding RNAs associated with larger, ribosomal components, and noncoding RNAs associated with low-molecular-weight complexes. The approach allowed the researchers to home in on the particular protein associated with a given RNA in order to uncover its function.

Smirnov, A. *et al. Proc. Natl. Acad. Sci. USA* **113**, 11591–11596 (2016).