STEM CELLS

Organoids that model the fetal placenta

Turco, M. Y. et al. *Nature* **564**, 263–267 (2018).

The placenta connects mother and fetus, enables nutrient and waste exchange, and performs other functions. For obvious reasons, this organ is difficult to study in humans. Turco et al. generated organoids that model the fetal contribution to the placenta, the trophoblast. The researchers defined conditions that allow the growth and propagation of these trophoblast organoids, thereby making it possible to maintain organoids for a year in culture. However, because the placental isolates used as the source material also contain maternally derived cells, care has to be taken to verify the fetal origin of the organoid cultures. The researchers confirmed the trophoblast nature of the organoids on the basis of previously established criteria such as marker gene and microRNA expression, as well as others. Furthermore, the organoids exhibited structural characteristics of the placenta and secreted appropriate metabolites and hormones. Trophoblast organoids could help researchers investigate placental development and disfunction. *NV*

https://doi.org/10.1038/s41592-019-0319-9

CELL BIOLOGY

Tagged reprogramming

Biddy, B. A. et al. *Nature* **564**, 219–224 (2018).

Direct reprogramming converts one somatic cell type to another, but the process is inefficient, which makes it difficult to study the molecular mechanism of lineage conversion. Biddy et al. use a lentiviral-based approach to label cells with barcode combinations that record both cell identity and clonal history. The researchers applied their 'CellTagging' to mouse embryonic fibroblasts, which they reprogrammed to endoderm progenitors (iEPs). After sequencing the tags and transcriptomes of over 80,000 cells, clustering them, and tracking iEP markers, they saw that many cells had initiated reprogramming but few completed the transition. They found that iEPs were derived from only a few clones, and lineage reconstruction showed a split in the trajectories, with one set of clones resulting in iEPs and the others resulting in a 'dead end'. This split occurred on day 6 of reprogramming, and expression of the methyltransferase Mettl17a1 was upregulated in the successfully reprogrammed clones. Knowing the contributors to direct reprogramming will help make the process more efficient. *NR*

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PROTEOMICS

Examining global RNA-binding proteomes

Trendel, J. et al. *Cell* **176**, 391–403 (2019).

Current methods for studying protein–RNA interactions focus mainly on either one protein, such as in CLIP-seq, or interactome capture involving only poly(A) RNAs, neither of which offers a full picture of how proteins interact with RNAs. Trendel et al. introduce a generic purification method for extracting global protein–RNA complexes, called XRNAX. They find that UV-cross-linked protein–RNA complexes are insoluble in the interphase of TRIZOL, a chemical solution that is widely used in RNA extraction. The complexes extracted from the interphase contain all major RNA biotypes and are enriched with RNA-binding proteins. To explore the RNA-bound proteome, one can carry out additional steps, including tryptic digest and silica column enrichment, to prepare the XRNAX extracts for mass spectrometry. The researchers applied XRNAX on three human cell lines (MCF7, HeLa, and HEK293), and identified over 700 proteins that interact with non-poly(A) RNAs. Moreover, XRNAX combined with CLIP-seq allows for further RNA sequencing to identify protein-binding RNAs. *LT*

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SENSORS AND PROBES

Tiny intracellular lasers

Fikouras, A. H. et al. *Nat. Commun.* **9**, 4817 (2018).

Fluorescent probes are widely used in biological imaging, but they are not ideal for all applications because they often have broad spectra, which limits multiplexing, and they can suffer from limited brightness and photostability. Intracellular lasers have recently been introduced that have narrow emission spectra and give bright and stable signal; however, these are larger than the average cell nucleus, which limits their utility. Fikouras et al. have developed semiconductor nanodisk lasers with volumes 1,000-fold smaller than the eukaryotic nucleus. Their small size is made possible by the large optical gain and high refractive index of their gallium indium phosphide/aluminum gallium indium phosphide multi-quantum well structure. Their lasing wavelength is size dependent, which makes the development of different-colored lasers straightforward. The nanodisk lasers were used as probes in several mammalian cell types. *RS*

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