TOOLS IN BRIEF

STEM CELLS

Stem cells tip toward totipotency

Early in mammalian development, cells that will form embryonic tissues distinguish themselves from those that will form extraembryonic tissues. Existing culture methods cannot typically maintain cells in the high state of pluripotency that exists prior to this split, but Yang *et al*. have found a way to generate mouse stem cells with expanded potential. The researchers derived cell lines by culturing single cells from embryos in either the four-cell or eight-cell stage in a medium that blocks blastomere development using small-molecule inhibitors of mitogen-activated protein kinases (MAPKs), Src and Hippo pathways. The extended pluripotent stem cell (EPSC) lines contributed to both inner cell mass (embryonic) and trophectoderm (extraembryonic) tissue and could differentiate into any blastomere lineage. In addition, the culture medium could even induce greater extraembryonic potential in existing pluripotent stem cell lines.

Yang, J. *et al*. *Nature* **550**, 393–397 (2017).

IMAGING

Tracking cell migration *in vivo*

Cells migrate throughout tissues as a normal part of development and maintenance. Most methods for tracking cell migration involve live imaging, which has provided crucial mechanistic understanding but can have unwanted effects on the physiology of an organism. To bypass some of these limitations, Chen *et al*. have developed a tool called M-TRAIL (matrix-labeling technique for real-time and inferred location) for tracing migration histories in fixed tissues. In M-TRAIL, migrating cells are engineered to express fluorescent-protein-tagged components of the basement membrane, which are secreted and deposited into the extracellular matrix as the cell migrates, and this marks the path of migration in a way that allows quantification of migratory dynamics. M-TRAIL was demonstrated in the *Drosophila* egg chamber, where the team was able to validate the hypothesis that tissue rotation is required for elongation.

Chen, D. *et al*. *Cell Rep*. **21**, 559–569 (2017).

GENOMICS

Haplobank of mutated mouse stem cell clones

When trying to understand the function of a gene, ideally a clone carrying a mutation is compared with an otherwise identical clone that carries the wild-type gene. Current mutagenesis approaches, while able to efficiently introduce mutations, do not easily produce pools of clones that vary only in a single mutation. An international team of researchers led by Ulrich Elling and Josef Penninger from the Institute of Molecular Biotechnology of the Austrian Academy of Sciences systematically targeted 16,970 mouse genes in haploid embryonic stem cells (ESCs) with barcoded vectors to achieve insertional mutagenesis. Flanking recombination sites allowed for two reversals of the vector, which made it possible to restore wild-type gene expression followed by another inactivation of the gene. The team used the resource to, for example, profile genes needed for resistance to a common cold virus. Clones are available at https://www.haplobank.at/.

Elling, U. *et al*. *Nature* **550**, 114–118 (2017).

BIOCHEMISTRY

A yTRAP for protein aggregates

Protein aggregation can cause devastating neurodegenerative diseases, but researchers are discovering that aggregation also plays a role in normal cellular function. A lack of high-throughput, quantitative tools for protein aggregation analysis has made this phenomenon challenging to study. Newby *et al*. now present yTRAP (yeast transcriptional reporting of aggregating proteins), a synthetic genetic platform that tracks protein aggregation states. The solubility state of a protein of interest is coupled to a synthetic transcriptional output; when the protein is in a soluble state, a fluorescent reporter is turned on; when aggregated, the reporter is turned off. The researchers demonstrate the use of yTRAP for sensing yeast prions in live cells, for screening mutant prion libraries to find prions that prevent aggregated states, and for identifying factors that affect aggregation of RNA-binding protein.

Newby, G.A. *et al*. *Cell* **171**, 966–979 (2017).