TOOLS IN BRIEF

CHEMICAL BIOLOGY

Snapshots of polyadenylation

Extracellular signaling molecules can promote translation by inducing polyadenylation, the addition of a poly(A) tail to mRNA. However, current methods cannot distinguish between mRNA molecules polyadenylated as a result of an external stimulus and those with preexisting poly(A) tails. In order to specifically identify those transcripts polyadenylated in response to a stimulus, Curanovic *et al.* synthesized an adenosine analog that is selectively incorporated into poly(A) tails. This alkyne-containing analog is incorporated into RNA by the existing machinery in living cells, allowing click-chemistry–based purification. The researchers used deep sequencing to identify 1,737 transcripts polyadenylated in oocytes in response to progesterone treatment, which activates oocyte maturation. This tool and method allowed them to perform an in-depth investigation of RNA sequence motifs associated with polyadenylation.

Curanovic, D. *et al. Nat. Chem. Biol.* doi:10.1038/nchembio.1334 (1 September 2013).

GENOMICS

A mutation for every worm gene

In a joint effort, researchers at one US and two Canadian institutions created 2,007 mutagenized *Caenorhabditis elegans* strains with alterations in each of the worm's more than 20,000 genes. Exposing the nematodes to a combination of two chemical mutagens and then selecting and propagating them for ten generations resulted in homozygous mutant strains with different types of mutations such as single-nucleotide variants, insertions and deletions, or large chromosome rearrangements. The researchers mapped each mutation to the worm genome to infer its effect. This resource will allow detailed studies of the role of particular genes in worm physiology. The Caenorhabditis Genetics Center will distribute the strains, and all sequences are available from WormBase.

Thompson, O. *et al. Genome Res.* **23**, 1749–1762 (2013).

LAB-ON-A-CHIP

A microchemostat array for yeast proteomics

The *Saccharomyces cerevisiae* GFP fusion library is an important tool for monitoring changes in protein abundance and localization in single cells in response to a perturbation. Dénervaud *et al.* harnessed this library to examine the global, dynamic behavior of the yeast proteome in response to DNA replication stress induced by methyl methanesulfonate (MMS). They developed a microfluidic platform consisting of 1,152 independent microchemostats for large-scale yeast strain analysis by fluorescence imaging, using a custom software pipeline to carry out all image processing steps. They captured movies of 4,085 GFP-tagged strains (1.5×10^8 cells in total), allowing them to discern substantial protein abundance changes for 124 proteins upon MMS treatment as well as localization changes for 118 proteins. They further examined a set of 506 deletion-GFP strains to identify components regulating processing-body formation upon ultraviolet irradiation.

Dénervaud, N. *et al. Proc. Natl. Acad. Sci. USA* **110**, 15842–15847 (2013).

MOLECULAR ENGINEERING

Highly accurate Cre variants

Site-specific recombinases offer benefits for integrating transgenes into a genome because they avoid the random and potentially mutagenic nature of transposon or viral insertion and they do not stimulate the mutagenic repair processes that targeted nucleases can trigger. However, altering recombinases to recognize new sequences for gene delivery usually leads to nonspecific activity. Eroshenko and Church used theoretical modeling to show that reducing the binding cooperativity of the Cre recombinase dimer can improve binding accuracy without affecting the protein interface that determines the DNA-binding sequence. Using bacterial selection, they identified three Cre mutants that efficiently recombine *loxP* sites with fewer off-target events in the *Escherichia coli* genome.

Eroshenko, N. & Church, G.M. *Nat. Commun.* **4**, 2509 (2013).