TOOLS IN BRIEF

GENOMICS

Sequencing the end

Alternative polyadenylation (poly(A)) adds to transcript variety as several sites within the 3′ UTR of a transcript can be chosen as recipients of the poly(A) tail. Some of these alternative poly(A) sites are important for normal development and disease; this prompted researchers to develop high-throughput methods to detail all poly(A) occurrences in the transcriptome. The PolyA-seq approach of Derti *et al.* captures the sequence immediately upstream of the poly(A) tail in a strand-specific and quantitative manner. Through their analysis of 24 tissues in five mammalian species, the researchers increased the number of known poly(A) sites in human cells by over 50% and showed that almost 70% of human genes have more than one poly(A) site in their 3′ UTR. This vast catalog of poly(A) sites will provide insight into evolutionary conservation of sites and provide a rich resource for studying the tissue-specific functions of alternative polyadenylation.

Derti, A., *et al. Genome Res.* advance online publication (18 April 2012).

BIOPHYSICS

Probes to detect strain

Cells *in vivo* exist within a complex and dynamic biophysical milieu. Forces exerted by cells on the surrounding extracellular matrix (ECM) and vice versa are thought to play an important role in normal function and disease. However, there are few methods to monitor ECM strain, particularly within tissue. Cao *et al.* report using phage display to identify peptides that can discriminate between relaxed and strained forms of fibronectin. They screened a phage-display library for peptides that bound fibronectin subjected to varying amounts of mechanical strain on PDMS surfaces *in vitro* and identified two such discriminatory probes that had complementary specificity. Fluorescently labeled versions of the phages—or of peptides derived from them—distinguished between relaxed and strained fibronectin *in vitro* and showed different binding patterns in *ex vivo* mammalian tissue.

Cao, L. *et al. Proc. Natl. Acad. Sci. USA* advance online publication (23 April 2012).

CHEMICAL BIOLOGY

Rapamycin's sister

Rapamycin is the most commonly used agent for chemically induced dimerization of fusion proteins. Since its discovery, there has been interest in finding other molecules applicable in alternative chemical dimerization systems for orthogonal use with rapamycin. Miyamoto *et al.* recently found one such molecule, GA_3, among the family of plant gibberellin hormones. The authors optimized GA_3 for cellular uptake and fused target proteins to GA_3's receptor, GID1, and its interacting partner GAI. The gibberellin system acts on a timescale of seconds and, in combination with rapamycin-based protein control, can be used to generate intersectional gates in cells.

Miyamoto, T. *et al. Nat. Chem. Biol.* **8**, 465–470 (2012).

SENSORS AND PROBES

Tag, you're orange

Imaging the interaction of multiple proteins tagged with different genetically encoded fluorescent proteins can require complex and expensive optical setups. One solution is to use fluorophores with a large Stokes shift between excitation and emission so that a single laser can be used to excite a number of markers with distinct emission wavelengths. Shcherbakova *et al.* filled a gap in the fluorophore spectrum by using random mutagenesis and directed evolution to engineer a bright monomeric orange fluorescent protein with a large Stokes shift, LSSmOrange (excitation/emission 437/572 nm). They demonstrated the utility of LSSmOrange by imaging four proteins simultaneously using fluorescence cross-correlation spectroscopy *in vitro*. They also designed two compatible pairs of Förster resonance energy transfer reporters to concurrently monitor calcium spikes and apoptosis in HeLa cells.

Shcherbakova, D.M. *et al. J. Am. Chem. Soc.* advance online publication (24 April 2012).