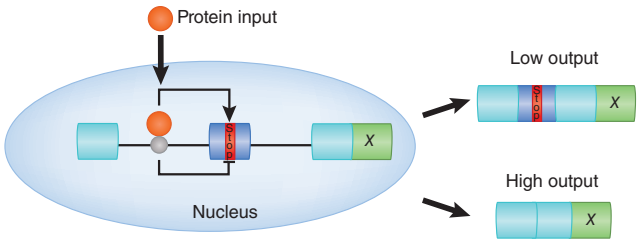


Mechanism of action of RNA controllers. Binding of the protein input to the sensor alters the splicing pattern of the RNA molecule by enhancing or suppressing alternative exon exclusion, resulting in different production levels of the gene of interest, *X*.

These RNA-based devices are not only one of the first ones demonstrated to respond to native proteins but also, because they are based on the use of alternative splicing, they offer endless possibilities for gene-expression regulation. One could imagine future developments of more complex types of controllers based on similar strategies as the one used by the Smolke group. For example, by regulating the inclusion of exons that actually encode for functional protein domains, one could control what splicing variant of a protein is produced or where it is localized in the cell. Bioengineering and synthetic biology are rapidly growing fields and their application to biological studies will enable fine control of cellular function and also aid in further refining these promising techniques.

**Erika Pastrana**

**RESEARCH PAPERS**

Culler S. J. *et al.* Reprogramming cellular behavior with RNA controllers responsive to endogenous proteins. *Science* **330**, 1251–1255 (2010).

researchers could even piece together new biosynthetic pathways underlying the production of several nucleotide variants.

However, they also encountered unexpected complexity, with many apparent disparities between the biochemical and genetic data. For example, even though levels of nucleotide variant $M^2_2G$ increased in response to hydrogen peroxide, cells lacking tRNA methyltransferase 1, the enzyme responsible for this particular modification, were not notably sensitized to hydrogen peroxide treatment. Dedon points out that clarifying the mechanistic explanations for these seeming contradictions and delving deeper into how these pathways specifically intersect and interact to achieve specific biological outcomes will be primary objectives for future work. The resulting data will ultimately be incorporated into a publicly accessible repository.

In parallel, they are also moving outside of eukaryotic organisms to explore the extent to which pathogenic bacteria may exploit such modification pathways to flourish in their hosts. "When a macrophage produces reactive nitrogen species, how do bacteria respond to these toxic chemicals in terms of translational control mechanisms?" asks Dedon. "We're very eager to look at the microbial side of this whole RNA modification story."

**Michael Eisenstein**

**RESEARCH PAPERS**

Begley, U. *et al.* Trm9-catalyzed tRNA modifications link translation to the DNA damage response. *Mol. Cell* **28**, 860–870 (2007).

Chan, C.T.Y. *et al.* A quantitative systems approach reveals dynamic control of tRNA modifications during cellular stress. *PLoS Genet.* **6**, e1001247 (2010).

## NEWS IN BRIEF

**BIOCHEMISTRY**

### An RNA crystallization chaperone

The crystallization of RNA molecules for structural analysis is even more challenging than protein crystallization owing to the low chemical diversity, flexibility and conformational heterogeneity of RNA. Koldobskaya *et al.* introduce a chaperone system that stabilizes RNA structure and promotes crystallization. The chaperone is an antigen-binding fragment (Fab) that recognizes an epitope tag that can be installed on any RNA of interest.

Koldobskaya, Y. *et al. Nat. Struct. Mol. Biol.* **18**, 100–106 (2011).

**BIOPHYSICS**

### Video force microscopy

Brodland *et al.* introduce a technique called video force microscopy, which is used to noninvasively generate detailed force maps of tissues from time-lapse multiphoton images. The method involves discretizing tissue into polygonal regions and tracking the corners of these regions to quantify deformations, allowing the user to determine whether the deformations are a result of active or passive forces. Brodland *et al.* used the method to measure the driving forces responsible for ventral furrow formation in *Drosophila melanogaster* embryos.

Brodland, G.W. *et al. Proc. Natl. Acad. Sci. USA* **107**, 22111–22116 (2010).

**EPIGENETICS**

### Distribution of 5-hydroxymethylcytosine in the genome

As 5-hydroxymethylcytosine (5-hmC) is a recently discovered epigenetic modification, little is currently known about its distribution and functional roles. Song *et al.* have now developed a method for mapping the genome-wide distribution of 5-hmC. The method involves using a β-glucosyltransferase to transfer a glucose containing an azide handle onto 5-hmC; the azide can then be tagged with biotin for enrichment and sequencing of the captured DNA fragments containing 5-hmC.

Song, C.-X. *et al. Nat. Biotechnol.* **29**, 68–72 (2011).

**PROTEOMICS**

### Protein-lipid interactions

Besides building cellular membranes, lipids operate as important signaling molecules via their interactions with proteins, but knowledge of these interactions is incomplete. Gallego *et al.* report a systematic, unbiased screening approach to identify protein-lipid interactions in the yeast *Saccharomyces cerevisiae* by detecting protein binding to miniature lipid arrays. Gallego *et al.* identified 530 protein-lipid interactions, most of which were previously unknown.

Gallego, O. *et al. Mol. Syst. Biol.* advance online publication, 30 November 2010.

**CELL BIOLOGY**

### Carbon nanotube endoscopes

Glass pipettes are useful tools for making electrophysiological measurements and injecting substances into cells, but because of their large size they can damage the cell. Singhal *et al.* introduce a carbon nanotube–based 'endoscope', 10 times smaller than a typical glass pipette, which can be used to probe cells with 100-nanometer spatial resolution, including intracellular organelles. The endoscope can also be used to deliver fluids to the cell, something previous carbon nanotube–based probes could not do.

Singhal, R. *et al. Nat. Nanotechnol.* **6**, 57–54 (2011).