TOOLS IN BRIEF

PROTEOMICS

RNA and the proteins that bind

To understand how RNA exerts its many functions, one needs to understand which proteins it interacts with. The study of RNA-binding proteins (RBPs) has occupied scientists during the last two decades, and the more recent combination of cross-linking and immunoprecipitation (CLIP) with high-throughput sequencing has provided a better understanding of RNA-binding motifs. Two independent research efforts now substantially add to the catalog of known RBPs in human cells. By pairing methods similar to photoactivatable ribonucleoside-enhanced CLIP with quantitative proteomics, Baltz *et al.* identified around 250 new RBPs in human embryonic kidney cells and derived protein occupancy profiles by high-throughput sequencing, and Castello *et al.* added more than 300 new RBPs from HeLa cells to the existing repertoire.

Baltz, A.G. *et al. Mol. Cell* **46**, 674–690 (2012).

Castello, A. *et al. Cell* **149**, 1393–1406 (2012).

SENSORS AND PROBES

Synaptic activity shines in red

Our understanding of the complex physiology of neurons can be greatly aided by the use of genetically encoded, fluorescent reporters. The turnover of vesicles that occurs in neuronal synapses, for example, signals the transmission of electrochemical signals between neurons. This process can be monitored using a pH-sensitive variant of GFP called pHluorin. But because many other activity-based reporters are also based on GFP, they cannot easily be used together. Li and Tsien engineered a pH-sensitive red fluorescent protein, dubbed pHTomato, which can be used in combination with other probes based on GFP. They used it to make a reporter of activity-dependent vesicle membrane fusions. By coupling pHTomato and GFP-based probes, they demonstrate the possibility of all-optical neurophysiology studies.

Li, Y. & Tsien, R.W. *Nat. Neurosci.* **15**, 1047–1053 (2012).

CHEMICAL BIOLOGY

Shutting down parts of the glycome

The transfer of a fucose or sialic acid sugar to a growing polysaccharide represents one step in a complex process that is poorly understood. Twenty sialyltransferases and 14 fucosyltransferases encoding variable acceptor specificities, activities and expression patterns are encoded in the human genome. To date, fluorinated analogs that block the transition state of these enzymes have not been membrane permeable, prompting Rillahan *et al.* to modify them by peracetylation. These protected analogs are neutrally charged and can slip into the cell, where sialic acid and fucose salvage pathway enzymes revert them to their unprotected form. The resulting membrane-permeable, family-specific inhibitors also shut down new biosynthesis through metabolic feedback, making them promising tools for dissecting the roles of fucosylated and sialylated glycans in cell communication and immunity.

Rillahan, C.D. *et al. Nat. Chem. Biol.* **8**, 661–668 (2012).

GENE EXPRESSION

Long noncoding RNAs in the worm

Long noncoding (lnc) RNAs go by different names depending on their genomic origin: long intervening, or intergenic, RNAs are far from any coding region; antisense noncoding RNAs, also known as natural antisense transcripts, are transcribed from the antisense strand of a gene. Only a fraction of lncRNAs have been functionally characterized to date, and for many organisms, an exhaustive catalog of all lncRNAs is still missing. *Caenorhabditis elegans*, one of the model organisms studied by the modENCODE consortium, now has over 64,000 annotated transcripts, which Nam and Bartel reanalyzed to arrive at a catalog of long intervening and antisense noncoding RNAs expressed at various stages of the nematode's development. Knowing more about genomic location, conservation and expression of these lncRNAs will aid in better understanding their roles.

Nam, J.-W. & Bartel, D.P. *Genome Res.* published online (15 June 2012).