METHODS IN BRIEF

IMAGING

Mass spectrometry imaging with MALDI-2

Matrix-assisted laser desorption/ionization (MALDI)-based mass spectrometry imaging is used to image the distribution of various biological molecules in tissue slices, thus providing both spatial and molecular information. A limiting factor, however, has been the low sensitivity of the technology, a result of poor ionization; on average, just 1 out of 1,000 biomolecules that is desorbed is ionized. Soltwisch *et al.* report a strategy called MALDI-2, which improves the sensitivity of MALDI imaging by up to two orders of magnitude. In MALDI-2, a wavelength-tunable positionization laser initiates a secondary ionization process in the gas phase. This allowed the authors to identify many more biomolecules—including various lipid species, fat-soluble vitamins, oligosaccharides and glycosides—imaged in both plant and animal tissue, with a very high lateral resolution of 5 micrometers.

Soltwisch, J. *et al. Science* **348**, 211–215 (2015).

GENOMICS

ChIP-nexus detects transcription factor binding sites

To understand how transcription factors (TFs) exert their control over gene expression, it is important to characterize their precise binding sites on DNA. Although the resolution of traditional chromatin immunoprecipitation (ChIP) is limited to the size of the DNA fragment containing the binding site, a recent improvement, ChIP-exo—in which one strand is digested by an endonuclease to the first base pair involved in TF binding—provides much higher resolution. He *et al.* now add a self-circularization step to the ChIP-exo protocol. Their ChIP-nexus technique is more efficient and produced higher quality data than ChIP-exo for several TFs. Because of its high resolution, ChIP-nexus could be used to investigate the effect of single-nucleotide variants, nucleosomes or DNA methylation in TF binding.

He, Q. *et al. Nat. Biotechnol.* **33**, 395–401 (2015).

MOLECULAR BIOLOGY

A TRICK for studying translation

The spatiotemporal regulation of translation is crucial for proper gene expression. Halstead *et al.* describe a new tool for monitoring the kinetics of the first round of translation. This method, translating RNA imaging by coat protein knock-off (TRICK), allows researchers to distinguish between the translated and untranslated forms of an mRNA of interest in a living cell. In TRICK, an mRNA is dual labeled in the coding region and the 3′ untranslated region using site-specific RNA-binding proteins fused to fluorescent proteins (PP7-GFP and MS2-RFP, respectively). Upon translation, the PP7-GFP bound in the coding region is displaced by the ribosome, leaving only red fluorescence signal. Applying the method in *Drosophila* oocytes, the researchers showed that mRNAs are not translated in the nucleus but translated within minutes after export.

Halstead, J.M. *et al. Science* **347**, 1367–1371 (2015).

BIOCHEMISTRY

Fast reaction kinetics with time-resolved mass spectrometry

A variety of approaches have been developed to study very fast chemical reaction kinetics in solution, including fast mixing in microfluidics devices, phototriggered reaction initiation and temperature-jump methods. Mass spectrometry can be used as the readout for characterizing the kinetics of rapid reactions, but it has been limited to millisecond time resolution. Lee *et al.* report an approach that improves the temporal resolution to as low as 3 microseconds, as applied to the study of the acid-induced unfolding of cytochrome *c* and the hydrogen-deuterium exchange reaction of the short peptide bradykinin. They achieved this excellent time resolution by colliding two streams of microscopic liquid droplets using pressurized nitrogen gas, thereby allowing rapid droplet fusion. The droplets are then directed to a mass spectrometer to determine the masses of the reaction intermediates and their products.

Lee, J.K. *et al. Proc. Natl. Acad. Sci. USA* **112**, 3898–3903 (2015).