METHODS IN BRIEF

SEQUENCING

Targets of RNA cytosine methyltransferases

RNA is methylated at specific cytosine residues. The modification occurs mainly in noncoding species such as tRNA and rRNA and is carried out by methyltransferases that form a transient covalent bond with their target cytosines. Khoddami and Cairns use 5-azacytidine, a cytidine analog that can be incorporated into RNA by living cells, to render the bond permanent, which allows the enzyme and its bound targets to be enriched by immunoprecipitation. 5-Azacytidine also causes C-to-G changes at methylation target sites; as a consequence, targets can be precisely located through sequencing of the enriched RNA. Starting with overexpressed tagged methyltransferases DNMT2 and NSUN2, the researchers enriched known target sites over 200-fold and discovered new targets in human cancer and fibroblast cell lines.

Khoddami, V. & Cairns, B.R. *Nat. Biotechnol.* **31**, 458–464 (2013).

CHEMISTRY

Reaction discovery by mass spectrometry

Discovery of novel chemical reactions is a fundamental focus of the field of organic chemistry. Cabrera-Pardo *et al.* report a high-throughput methodology for reaction discovery, using the power of laser desorption/ionization mass spectrometry (MS). In this approach, the researchers place an inert, polyaromatic MS label on a reactant such that any products that form will also contain the label. This facilitates their easy detection in the resulting mass spectrum without requiring purification. The authors carefully selected an MS label that would also promote selective desorption/ionization so as to circumvent the need for a typical matrix, which would make low–molecular weight products difficult to detect by MS. Applying the method to screen nearly 700 different reactant combinations, they discovered two novel benzannulation reactions, which may find use in organic synthesis.

Cabrera-Pardo, J.R. *et al. Nat. Chem.* **5**, 423–427 (2013).

GENOMICS

Population genomics without a reference

To understand molecular evolution, researchers seek to analyze genomic variation, mutation rate and effective population size within a species and then compare the findings between species. These studies have required well-annotated genomes, and for metazoans they have been mainly restricted to humans and drosophilids. For a deeper understanding of evolution, genome-wide population studies from more diverse species are needed. Gayral *et al.* sequenced the transcriptomes of several individuals from two vertebrate species (hare and turtle) and three invertebrate species (oyster, termite and tunicate) and present a pipeline for cDNA assembly, read mapping and genotyping to perform *de novo* genome-wide population analysis. As predicted, they found higher genomic diversity in the invertebrates, but, surprisingly, they also saw that the ratio of nonsynonymous to synonymous mutations did not differ between the invertebrates and vertebrates, indicating that the efficiency of natural selection does not vary across the different phyla.

Gayral, P. *et al. PLoS Genet.* **9**, e1003457 (2013).

NANOBIOTECHNOLOGY

Polypeptide nanostructures

A variety of DNA-based nanostructures have been created by researchers taking advantage of base complementarity to rationally design folds. The engineering of polypeptide-based nanostructures is more challenging owing to the broader chemical diversity of amino acids, but this diversity should also permit greater design flexibility. Gradišar *et al.* report the design of a self-assembling tetrahedron (of about 7 nanometers in diameter) from a single polypeptide chain containing concatenated coiled-coil dimer-forming segments interspersed with flexible regions. Fletcher *et al.* describe design rules for forming large, spherical cages (of about 100 nanometers in diameter) self-assembled from a carefully chosen set of coiled-coil peptides. Such polypeptide-based nanostructures could be used for applications such as drug delivery or, in the case of the spherical cages, as potential 'protocells' in synthetic biology.

Gradišar, H. *et al. Nat. Chem. Biol.* doi:10.1038/nchembio.1248 (28 April 2013).

Fletcher, J.M. *et al. Science* **340**, 595–599 (2013).