TOOLS IN BRIEF

GENETICS

Gene correction with CRISPR in adult mice

The clustered, regularly interspaced, short palindromic repeats (CRISPR)-Cas9 system has been used for genome modification in many organisms, including for correction of disease-causing mutations in mouse zygotes. Yin *et al.* now report the use of CRISPR-Cas9 for mutation correction in the liver of adult mice that carry a point mutation in the gene encoding fumarylacetoacetate hydrolase (Fah), which causes acute liver damage and death. Delivery of a vector encoding a guide RNA targeting *Fah* and the Cas9 endonuclease, together with a single-stranded oligonucleotide carrying the desired mutation reversal, all to the liver, resulted in rescue of the animals as well as detectable Fah activity and gene correction. Methods remain to be developed for delivery and gene correction in other adult tissues.

Yin, H. *et al. Nat. Biotechnol.* doi:10.1038/nbt.2884 (30 March 2014).

NEUROSCIENCE

A large-scale approach to correlate neurons and behavior

Identifying the neural circuits behind even a single animal behavior has so far been a slow process. Vogelstein *et al.* describe a high-throughput approach for mapping multiple larval behaviors in *Drosophila melanogaster* to defined neurons. The researchers combined automated behavioral tracking with optogenetic activation via channelrhodopsin of 1,054 *Drosophila* lines having sparse neuronal expression patterns to analyze the behavior of about 38,000 fly larvae. Upon clustering the observed behaviors with a multiscale unsupervised structure-learning method, the researchers observed 29 distinct behaviors. Almost half of the fly lines behaved differently from controls, and in most lines, only one behavior was overrepresented. In conjunction with the morphological characterization available for these lines, the behavioral data provide a reference atlas for studying which neurons mediate which behaviors.

Vogelstein, J.T. *et al. Science* **344**, 386–392 (2014).

BIOPHYSICS

Machining better cantilevers

In atomic force microscopy (AFM) applications, cantilever choice heavily influences measurement performance. Two important characteristics are short-term force precision and long-term force stability. Previous work by Tom Perkins and colleagues showed that removing the gold coating from long cantilevers provided superior stability but that temporal resolution and force precision were not as good as with short cantilevers. Now, Bull *et al.* demonstrate how the removal of most of the arm of short cantilevers by focused-ion-beam milling increases long-term force stability and short-term force precision. The sensitivity conferred by the gold coating was retained by removing all of the gold except for in a region near the end that had no negative impact on stability. The modified cantilevers are relatively easy to make and provide high performance in a wide variety of applications, thereby eliminating most of the compromises inherent in cantilever choice.

Bull, M.S. *et al. ACS Nano* doi:10.1021/nn5010588 (26 March 2014).

CHEMICAL BIOLOGY

Chemical tools for yeast

Small molecules are useful tools for probing protein function in cells. Lee *et al.* report a large-scale screen characterizing the cellular response of yeast to a panel of 3,250 growth-inhibiting small molecules. They used a profiling approach called HIPHOP (haploinsufficiency profiling and homozygous profiling) to identify the protein targets of a small molecule by measuring fitness defects in a large number of heterozygous strains representing the essential genome and in an even larger number of homozygous deletion strains to identify non-essential genes that mitigate the effects of the small molecule. They identified 317 compounds that specifically affected the function of 121 genes. The yeast cells responded to the small molecules in just 45 different ways, which the researchers refer to as chemogenomic signatures. Lee *et al.* hypothesize that similar small-molecule response systems may be present across eukaryotic cells.

Lee, A.Y. *et al. Science* **344**, 208–211 (2014).