Finding real RNA editing sites

High-throughput sequencing has been a boon for the discovery of sequence variation, but analyzing data from short and error-prone reads is far from a trivial task. A recent spate of controversial studies claiming widespread differences between DNA and RNA from the same tissue source underlines the need for caution and the development of expert methods. In contrast to these studies, Li and colleagues failed to find verifiable evidence of differences between DNA and RNA outside of adenosine-to-inosine editing, which proceeds by a known mechanism, in human cell lines. Their computational pipeline carefully removes artifacts to detect true differences between matched genomic and transcriptomic sequence. The pipeline is a sensitive tool to discover bona fide RNA editing sites that greatly expand the coding potential of the transcriptome.

Brief Communication p579

The robotic patcher

Electrophysiology is among the hardest techniques in neuroscience to master. Whole-cell patch clamping, in which the tip of a Pasteur pipette is carefully inserted into a living cell to record the currents from its interior, requires a great deal of skill and labor, particularly when it is done in a living animal. Forest, Boyden and their collaborators have designed a robot that automatically performs patch clamping in mouse brains in vivo. The robot, called the ‘Autopatcher’, succeeded at making high-quality recordings from cells about one-third of the time, which is similar to what a trained investigator would achieve. This technology might make electrophysiology much more accessible to scientists.

Brief Communication p585

Improved genome editing

Targeted genome editing with engineered nucleases has huge potential as a research tool. Methods for effective nuclease assembly and for increasing the range of targetable genomic sequences are very desirable. In this issue, Wolfe and colleagues describe a validated archive of two-finger modules for assembling zinc-finger nucleases (ZFNs). The modules were selected for binding to target DNA sequences with all possible 2-bp junctions at the finger-finger interface. It comprises the largest set of ‘non N-G’–recognizing fingers to date and has increased target site density in the fish and human genomes. In the Research Highlights (p529), we discuss other recent improvements in genome editing tools, including ZFN ‘nickases’ for targeted single-strand cleavage and automated assembly of TAL-effector nucleases.

Brief Communication p575

Hybrid fluorescence–X-ray tomography

Fluorescence imaging in vivo is extremely challenging on account of light absorption and scattering by tissue. Tomographic methods use mathematical models of light propagation to correct for these effects, yielding three-dimensional fluorescence distributions in tissue, but their performance has limitations; the use of anatomical information from another imaging modality can help. In this issue, Ntziachristos and colleagues demonstrate the performance of a 360° hybrid fluorescence and X-ray tomographic system for in vivo imaging in the mouse. They implement a method for user-independent reconstruction of the fluorescence distributions and validate their results by imaging the corresponding cryoslices from the same animals. They apply this hybrid method to image three mouse models of disease.

Article p615

More neurons per skin cell

In an era of malleable cell identities, turning a skin cell into a neuron is no longer news. However, obtaining a high number of neuronal cells with these protocols remains a challenge. Until now, methods for direct neuronal conversion of mouse and human fibroblasts using particular combinations of transcription factors yielded only a small fraction of neuronal cells from the total population. Brüstle, Koch and their collaborators optimized these protocols by adding to the medium a combination of small molecules known to have a role in neural induction. They show that this recipe increases the percentages of neurons obtained from human postnatal fibroblasts by more than 15-fold.

Brief Communication p575