the variable differentiation behavior there may be some differences in the pluripotent state.

They went on to examine many more cell lines, including both hESC and hiPSC lines, and found, in a retrospective analysis but importantly also prospectively, that expression of the *miR-371* cluster is predictive of neural differentiation. In other words, the researchers could predict the neural differentiation behavior of cell lines, via two entirely different differentiation protocols, purely on the basis of expression of *miR-371*. Specifically, they saw that lines with low *miR-371* expression are more neurogenic. Expression of this marker could also predict which stem cell lines could give rise to dopaminergic neurons that stably engraft *in vivo*.

Although Studer and colleagues had clearly identified a practically useful marker, they were also interested in the underlying biology. "We didn't really know when we began," Studer says, "if we would find random markers that for whatever reason mark a certain behavior or if there would be some logic behind it that would tell us why the cells behave differently." As it turns out, understanding the role of the *miR-371* cluster in differential stem cell behavior is somewhat complicated. The marker distinguishes between cell lines with different requirements for bone morphogenic protein (BMP) signaling in neural induction, but the finer details of its role will require additional studies.

In the meantime however, it should prove practically useful to identify human pluripotent stem cell lines that enthusiastically make neurons, and suggests that similar markers may be identified that are predictive for differentiation to other cell types.

Natalie de Souza

RESEARCH PAPERS

Kim H. *et al.* miR-371-3 expression predicts neural differentiation propensity in human pluripotent stem cells. *Cell Stem Cell* **8**, 695–706 (2011).

so that multiple steps could be conducted in 96-well plates without the need to grow and select clones between steps. They subjected a bacterial artificial chromosome to three rounds of modification, purified the resulting plasmid and passed it through recombinase-expressing bacteria to generate an intermediate targeting vector. The final vector is assembled, conveniently, *in vitro*. Finally, they electroporate the vectors into a mouse embryonic stem cell line that contributes strongly to the germline and other tissues in chimeric mice (Pettitt *et al.*, 2009)

The technique should work for other mouse strains and even other species, says Skarnes. He and his colleagues are currently using this system to eliminate both copies of genes in embryonic stem cells to study gene function in a model cell.

But the real payoff will come not from engineering cells but from studying mice derived from them. That is why Skarnes is particularly excited that several international government bodies are supporting this task. "Once the cells are converted into mice," he says, "we, [scientists,] can start the real work, which is to understand gene function."

Monya Baker

RESEARCH PAPERS

Pettitt, S. J. *et al.* Agouti C57BL/6N embryonic stem cells for mouse genetic resources. *Nat. Methods* **6**, 493–495 (2009).

Skarnes, M.C. *et al.* A conditional knockout resource for the genome-wide study of mouse gene function. *Nature* **474**, 337–342 (2011).

NEWS IN BRIEF

MODEL ORGANISMS

Zinc-finger nucleases for gene correction *in vivo*

There a great deal of interest in the use of zinc-finger nucleases for tailored genome engineering, but they have not yet been used for genome modification *in vivo*. Li *et al.* now use zinc-finger nuclease–mediated targeting of a promoter-less DNA fragment to correct mutations in a mouse model of hemophilia B. They intraperitoneally injected a hepatotropic adeno-associated viral vector to deliver the nuclease and the therapeutic fragment, and observed sufficiently effective gene targeting to restore functional clotting in the mouse.

Li, H. *et al. Nature* advance online publication (26 June 2011).

MASS SPECTROMETRY

Introducing the Q Exactive

Michalski *et al.* introduce the Q Exactive, a benchtop mass spectrometer with many beneficial advantages for proteomics research. This instrument combines quadrupole and Orbitrap analyzers, allowing multiplexed operation for single-stage and tandem mass spectrometry. Compared to current top-of-the-line Orbitrap instruments, the Q Exactive also offers high mass spectrometric resolution, identifies more peptides in a single run and is faster and easier to use.

Michalski, A. *et al. Mol. Cell. Proteomics* advance online publication (3 June 2011).

STRUCTURAL BIOLOGY

Combined solution and solid-state NMR spectroscopy

Bertini *et al.* report a method for investigating the structure of large proteins by nuclear magnetic resonance (NMR) spectroscopy both in solution and in solid state without changing the sample tube. They first performed solution-state NMR measurements on the protein apoferritin. Then, by spinning the sample tube at ultracentrifugation speeds, the protein sedimented on the tube walls, allowing them to make solid-state measurements. The method is applicable to proteins larger than about 100 kilodaltons.

Bertini, I. *et al. Proc. Natl. Acad. Sci. USA* **108**, 10396–10399 (2011).

MOLECULAR ENGINEERING

A minimalist nuclear pore

Disordered Phe-Gly domains of nucleporins are thought to constitute the selectivity filter at the nuclear pore. Kowalczyk *et al.* report a biomimetic nuclear pore complex capable of selective protein transport. The minimalist structure consisted of a silicon-based nanopore coated with nucleoporin Phe-Gly domains. Stringency of selectivity depended both on nanopore diameter and the nucleoporin of choice, revealing intrinsic differences between nucleoporin function at the selectivity barrier.

Kowalczyk, S.W. *et al. Nat. Nanotechnol.* **6**, 433–438 (2011).

IMAGING

Fluorescent cell biolasers

Lasers emit light through optical amplification of input electromagnetic energy. This is achieved through stimulated photon emission by an appropriate "gain medium" inside a highly reflective optical resonator. By pumping single fluorescent cells with brief optical pulses in a mirrored biconcave microcavity, Gather and Yun could stimulate the emission of bright directional laser beams without affecting cell viability. The concept could enable new techniques for cellular and tissue imaging.

Gather, M.C. & Yun, S.H. *Nat. Photonics* **5**, 406–410 (2011).