and supports the idea that adult skin stem cells can be used as donors for nuclear transfer.

It has also been suggested that reprogramming by oocytes, and hence cloning efficiency, may vary inversely with differentiaton state. But as the researchers found no significant difference between birth rates for mice derived from female cumulus cells (a differentiated, somatic cell type) as compared to those derived from female bulge keratinocyte stem cells, there is no evidence in the study to support this idea, at least not in females.

An outstanding question in cloning by nuclear transfer is the very low efficiencies that are typically achieved. Mombaerts points out that now—almost ten years after the first mouse was cloned—it is still not clear to what extent this low efficiency is due to biological problems, such as failure to properly erase genomic imprints of differentiated cells, as opposed to technical problems, such as micromanipulation. But as Fuchs emphasized, "by the time a keratinocyte is a keratinocyte, it probably has all these epigenetic marks that say it is not pluripotent; it is a skin stem cell, and it is incredible to me that one can get rid of that at all." What distinguishes a reconstructed oocyte that will generate a healthy clone from one that will not, is a fascinating question that still remains to be answered.

Natalie de Souza

RESEARCH PAPERS

Li, J. *et al.* Mice cloned from skin cells. *Proc. Natl. Acad. Sci. USA* **104**, 2738–2743 (2007).

Notably, they observed different binding affinities for the purified NF-κB p50 versus that in cell extracts. "[You can] use the whole cell extract to look for the presence of other proteins that modulate the interactions about which you may not yet know," says Cantor.

One widely used method to investigate protein-DNA binding interactions *in vitro* is the gel shift or electrophoretic mobility shift assay. In this assay, binding interactions are determined by observing the retarded migration of a DNA sequence in complex with the target protein, in comparison to the free DNA sequence. Though gel shift is very popular, it is a relatively slow technique and carries the high risk of dissociation artifacts. In contrast, "The precision of being able to measure nucleic acid concentration in the mass spectrometer is unparalleled," says Cantor. "The second major advantage you get is sensitivity because mass spectrometry has no nonspecific background." Cantor believes that OMTs will also find use in other applications, for example, for highly sensitive multiplexed protein detection.

Allison Doerr

RESEARCH PAPERS

Gustafsdottir, S.M. *et al. In vitro* analysis of DNA-protein interactions by proximity ligation. *Proc. Natl. Acad. Sci. USA* **104**, 3067–3072 (2007).

Zhang, L. *et al.* Quantifying DNA-protein binding specificities by using oligonucleotide mass tags and mass spectroscopy. *Proc. Natl. Acad. Sci. USA* **104**, 3061–3066 (2007).

NEWS IN BRIEF

MICROFLUIDICS

Understanding the curious mating habits of yeast

The mitogen-activated protein kinase (MAPK) pathway in *Saccharomyces cerevisiae* is responsible for sensing mating pheromones sent out by other yeast cells. To investigate the quantitative regulation of the MAPK-regulated yeast pheromone response, Paliwal *et al.* developed a unique microfluidic device, which allowed them to load cells into test chambers, expose them to linear concentration gradients of pheromone, and monitor gene expression and phenotypic changes in individual cells.

Paliwal, S. *et al. Nature* **446**, 46–51 (2007).

PROTEOMICS

Label-free analysis of protein complexes

Rinner *et al.* describe MasterMap, a computational platform to aid in the quantitative analysis of protein complexes with label-free mass spectrometry. MasterMap is used to collect and compare multiple mass spectral analyses of protein complexes isolated via coimmunoprecipitation. Spectral features that differ from run to run, representing changes in interactions of the complex, can be selected for further analysis by tandem mass spectrometry. The approach is promising for large-scale protein interaction network mapping.

Rinner, O. *et al. Nat. Biotechnol.* **25**, 345–352 (2007).

GENOMICS

SNP discovery in non-model organisms

Single nucleotide polymorphisms (SNPs) are the most common type of genetic mutation. For non-model organisms with yet unsequenced genomes, however, SNP discovery is extremely difficult. Orsini *et al.* describe a method to detect and isolate SNP markers by exploiting the ability of the Mu transposition machinery to target mismatched DNA sites. The method led them to find 164 SNPs in the genome of the Glanville fritillary butterfly.

Orsini, L. *et al. Nucleic Acids Res.*; published online 20 February 2007.

CELL BIOLOGY

Crossing biological barriers with nanotubes

Carbon nanotubes are hot scientific property, with touted potential applications ranging from the industrial to the therapeutic. In a preliminary step toward characterizing their therapeutic potential, Kostarelos *et al.* performed an extensive study investigating the uptake of functionalized carbon nanotubes in a variety of cell types, including yeast and fungi.

Kostarelos, K. *et al. Nat. Nanotechnol.* **2**, 108–113 (2007).

SPECTROSCOPY

ssNMR spectroscopy for whole biological assemblies

Magic-angle spinning solid-state NMR (MAS ssNMR) spectroscopy is used in determining the structures of molecules that cannot easily be dissolved in solution, for example, of membrane-bound proteins. By using MAS ssNMR, Goldbourt *et al.* determined the secondary structure of the major coat protein subunit of the filamentous bacteriophage Pf1 on the intact phage, which retained infectivity after the NMR experiment.

Goldbourt, A. *et al. J. Am. Chem. Soc.* **129**, 2338–2344 (2007).