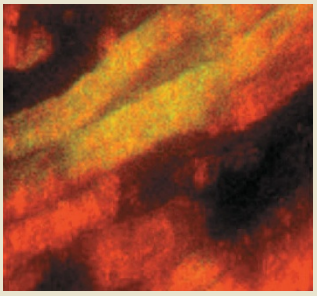
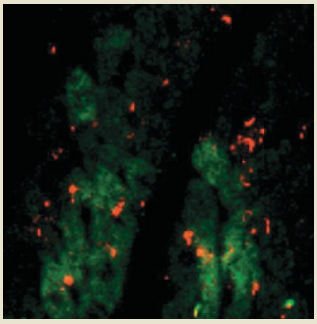
Made-to-order proteins

The expanded genetic code just moved up the evolutionary ladder. Using an approach similar to one they had worked out in bacteria, Peter Schultz and colleagues at the Scripps Research Institute (La Jolla, CA, USA) have expanded the genetic code of the eukaryote *Saccharomyces cerevisiae* (*Science* **301**, 964–967, 2003). The new code was derived from a bacterial amber suppressor tRNA synthetase–codon pair, which the authors further modified before introducing into yeast. Yeast transformed with such a mutagenized tyrosyl-tRNA synthetase–tRNACUA from *Escherichia coli* and fed unusual amino acids were able to incorporate five novel amino acids into protein, with each amino acid containing a tool for probing the structure or functions of proteins—a heavy atom for use in X-ray crystallographic studies, or probes for cross-linking proteins. Using this yeast system, the authors produced a modified human superoxide dismutase containing *p*-acetyl-L-phenylalanine, and showed that the purified human enzyme had incorporated the novel amino acid to 99.8% purity. The researchers intend to further expand the utility of this approach by applying other novel amino acids, such as those with spin labels or metal-binding sites. *LD*

Stem cells mend a broken heart



Mesenchymal stem cells (MSCs) isolated from bone marrow have been used to repair a heart damaged by heart attack. MSCs are self-renewing and can differentiate into several different cell types. Researchers have previously tried to repair damaged hearts with MSCs but achieved only limited success, in part because the cells die soon after transplantation. Writing in *Nature Medicine* (**9**, 1195–1201, 2003), Victor Dzau and coworkers from Brigham and Women's Hospital and Harvard Medical School (Boston, MA) describe how they inserted a gene for a survival-promoting signaling molecule, *Akt*, into MSCs and injected the cells into rats shortly after inducing heart attacks. The cells migrated toward injured myocardium and developed into cardiomyocyte-like cells that form connections with native myocytes. The researchers found that modified MSCs returned cardiac performance to near normal, restoring 80–90% of lost myocardial volume and preventing ventricular enlargement. It remains unclear how the cells heal the heart, but the results hold promise for the millions of people who suffer heart failure each year. *MS*



Research Notes written by Laura DeFrancesco, Andrew Marshall, Meeghan Sinclair and Gaspar Taroncher-Oldenburg.

Chip heats up protein analysis

Researchers have designed a microfluidics chip incorporating a thin polymer film that can trap and release proteins from solution according to temperature. Dale Huber and his colleagues at the Sandia National Laboratory (Albuquerque, NM) created their device (*Science* **301**, 352–354, 2003) by layering a 4-nm-thick film of polymer, poly(*N*-isopropylacrylamide), on top of an array of gold or platinum heater lines on a silicon chip. When at room temperature, the polymer is hydrophilic and repels proteins, such as myoglobin and albumin; in contrast, at temperatures above 35 °C, the film becomes insoluble, water is expelled and the polymer can adsorb proteins from solution. As the film returns to room temperature, it releases the proteins unharmed, with the entire process taking less than 1 second. The researchers claim the reversible protein adsorption could be used to separate soluble proteins in microfluidic devices or to create cost-effective chips for use in disease detection, blood typing and DNA sequencing. *AM*

Identifying sweet spots

One of the goals of proteomics is to generate comprehensive catalogs of classes of proteins sharing a specific function or modification. However, such efforts are often hampered by efficiency problems encountered during purification and separation of the target proteins from all other proteins present in the cell. Carolyn Bertozzi and colleagues at Lawrence Berkeley National Laboratory and the Howard Hughes Medical Institute, University of California, Berkeley (CA), have devised a strategy (*Proc. Natl. Acad. Sci. USA* 100, 9116–9121, 2003) to identify and separate one such class of proteins, the *O*-glycosylated proteins. These proteins fulfill essential roles as transcription factors, nuclear pore proteins and key metabolic enzymes in cells. The approach takes advantage of the ability of cells to use a glucosamine analog as a substrate for protein glycosylation *in vivo*. The analog, *N*-azidoacetylglucosamine, is metabolically incorporated into nuclear and cytoplasmic proteins, which are then covalently derivatized with a biochemical probe for their detection and further analysis. This approach provides a highly efficient tool to 'distill' the full component of *O*-glycosylated proteins from cells. *GTO*

Fighting blight

Potato late blight is one of the world's most devastating plant diseases. Caused by the pathogen *Phytophtora infestans*, late blight is responsible for substantial annual losses in potato and tomato production that can amount to spoiling of entire crops in countries with limited access to fungicides. In a recent issue of the *Proceedings of the National Academy of Sciences USA* (**100**, 9128–9133, 2003), Jiming Jiang and colleagues from the US Department of Agriculture, the University of Wisconsin (Madison, WI), the University of California, Davis and The Institute for Genomic Research (Rockville, MD) have now identified a potato gene that confers broad resistance to this disease. Working with a wild potato species that is highly resistant to all known races of *P. infestans*, the authors cloned the major resistance gene *RB* using standard genetic techniques. Transformation with the *RB* gene into the blight-susceptible potato variety Katahdin rendered the plants resistant to several highly infectious strains of *P. infestans* by significantly delaying and minimizing the spread of infection. *GTO*