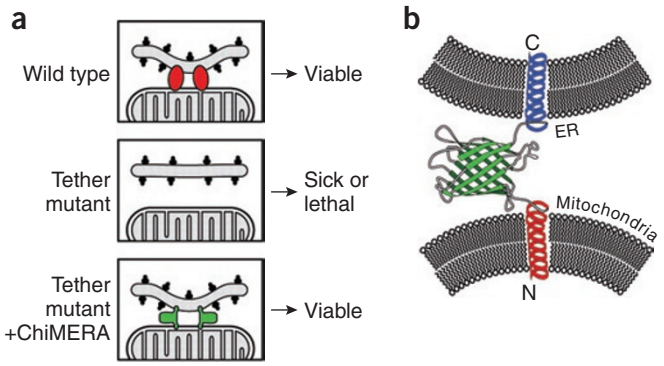

A synthetic ER-mitochondrial tether. (**a**) Mitochondria and ER are tethered by a native complex in yeast cells (top). Mutations to this complex cause slow growth or cell death (middle). A synthetic mitochondria-ER tether, ChiMERA, rescues cell growth (bottom). (**b**) The ChiMERA protein consists of an ER-directed domain (blue), a central GFP domain (green) and a mitochondria-directed domain (red). Reprinted with permission from The American Association for the Advancement of Science.

he says. Perhaps most interestingly, at least from a methods standpoint, the approach is also likely to have general value, as Kornmann explains: "If one is able to replace cellular function by an artificial protein—not necessarily tethering—any kind of function in principle should be amenable to doing this kind of method."

Allison Doerr

RESEARCH PAPERS
Kornmann, B. *et al.* An ER-mitochondria tethering complex revealed by a synthetic biology screen. *Science* **325**, 477–481 (2009).

given in familiar or unfamiliar surroundings.

Notably, this treatment did not appear to exert any nonspecific neurological effects, nor did it affect the rats' capacity to respond to cocaine or engage in normal locomotor activity. "It's a unique set of neurons that were only activated by the repeated presence of both the drug and the environment together," says Hope. "This means that it could be a mechanism for how the learned association is produced between those two factors."

His team is now investigating characteristics of the neurons affected in these experiments, but their initial findings suggest that Daun02 inactivation could offer a general strategy for precisely manipulating neural circuitry underlying other complex behavioral processes. Accordingly, Hope is now collaborating with National Institute on Drug Abuse colleague Yavin Shaham to apply their method to 'cue-induced reinstatement', the process by which certain environmental cues can restore seeking behavior in animals previously weaned off of drugs—in this case, heroin. "The parallel might be exposing an addict to drug paraphernalia, and all of a sudden they crave heroin," says Hope. "This is what that's supposed to model."

Michael Eisenstein

RESEARCH PAPERS
Koya, E. *et al.* Targeted disruption of cocaine-activated nucleus accumbens neurons prevents context-specific sensitization. *Nat. Neurosci.* **12**, 1069–1073 (2009).

NEWS IN BRIEF

SYNTHETIC BIOLOGY

Engineering *Escherichia coli* with new functions

Wang *et al.* present multiplex automated genome engineering (MAGE), a method to rapidly generate combinatorial genetic modifications by repeatedly introducing synthetic DNA to cells. The approach is based on the concept that for a pool of degenerate oligonucleotides, those with greater homology to the chromosomal target will be incorporated with higher frequency via allelic replacement. They applied MAGE to program *E. coli* to overproduce the antioxidant lycopene by optimizing the biosynthetic pathway.

Wang, H.H. *et al. Nature* **460**, 894–898 (2009).

CHEMICAL BIOLOGY

Multiplexed kinase activity profiling

Protein kinases have differential levels of activity under different biological conditions. Yu *et al.* describe an approach to profile the activation state of kinases in a cell lysate by monitoring the phosphorylation of 90 synthetic known peptide substrates via mass spectrometry, using heavy isotope–labeled versions of the peptides as internal quantitative standards. They applied the method to profile kinase activity during the cell cycle, in breast cancer cell lines and after applying kinase inhibitors.

Yu, Y. *et al. Proc. Natl. Acad. Sci. USA* **106**, 11606–11611 (2009).

NANOTECHNOLOGY

Fluorescent-plasmonic nanoparticles

Jin and Gao describe an approach to make multifunctional nanoparticles that are both fluorescent and plasmonic. This presented a challenge because gold, the plasmonic material, can quench fluorescence. Jin and Gao overcame this by precisely controlling the spacing between a quantum dot core and an ultrathin gold shell via layer-by-layer assembly.

Jin, Y. & Gao, X. *Nat. Nanotechnol.* advance online publication (26 July 2009).

PROTEOMICS

The Dub interactome

Although the ubiquitin conjugation machinery is fairly well understood, the functions of deubiquitinating enzymes (Dubs), which catalyze the removal of ubiquitin from proteins, have not been vastly studied. Sowa *et al.* profiled the human Dub protein family using an affinity purification scheme followed by mass spectrometry to analyze Dub protein interaction partners. They also introduce CompPASS, a software platform for identifying high-confidence interactions.

Sowa, M.E. *et al. Cell* **138**, 389–403 (2009).

BIOPHYSICS

Transcription initiation on a single-molecule scale

Single-molecule fluorescence resonance energy transfer can be used to monitor molecular motions over time, but multiplexing is limited. Sorokina *et al.* describe a single-molecule method that requires only a single fluorophore, using time correlated single-photon counting for monitoring fluorescence lifetime trajectories of an immobilized molecule. They used this approach to follow the complex process of transcription initiation by T7 RNA polymerase.

Sorokina, M. *et al. J. Am. Chem. Soc.* **131**, 9630–9631 (2009).