indeed, bioinformatic analysis of existing sequence data for both Myc binding and for epigenetic marks at the promoter of the miR-290 cluster, supports this idea. Experimental testing of the possible mechanisms of microRNA function is ongoing, but Blelloch cautions that it will be difficult to tease out the function of individual microRNAs. "There are three microRNAs in the miR-290 cluster that share the same seed sequence, and that is just the beginning; there are other clusters as well, miR-17, for instance. And we know from our previous work that the system is incredibly redundant. In embryonic stem cells, we identified 11 microRNAs with the same seed sequence that were all interchangeable in their function," he says.

Could microRNAs replace all transcription factors in the reprogramming process? Blelloch is doubtful, but points out that even replacement of some of them would be beneficial, and screens for such factors are in progress in his laboratory. Others have also reported the use of both cell-penetrating recombinant proteins—in recent work from the laboratory of Sheng Ding at the Scripps Institute (Zhou *et al.*, 2009)—and small molecules, to achieve reprogramming. "Ultimately the goal is to use some mix of factors to replace DNA elements altogether," Blelloch states, "and I think that will happen, but what the final cocktail will be remains to be seen."

Natalie de Souza

RESEARCH PAPERS

Judson, R.L. *et al.* Embryonic stem cell–specific microRNAs promote induced pluripotency. *Nat. Biotechnol.* **27**, 459–461 (2009).

Zhou, H. *et al.* Generation of induced pluripotent stem cells using recombinant proteins. *Cell Stem Cell* **4**, 381–384 (2009).

Integrating the results from the proteomics experiments and genomic context analysis, the researchers generated a dataset of high-confidence pairwise interactions for 99% of the annotated and 96% of the unannotated genome. "Is protein-complex information or genomic context enough to tell you about a protein's role in the cell? No, but it certainly gives you hints," says Emili. They created a function prediction tool called StepPLR to assign putative functions to the orphans, using the information about 'whom' the orphans interacted with, directly and indirectly. Notably, they predicted that many of the orphans are actually involved in core cellular processes. Emili hopes that *E. coli* researchers with proteins or genes or pathways of interest will follow up on their functional predictions.

The researchers have set up a public resource called eNet to host their data, and they plan to keep adding to it and refining it. "It's not a complete story; we'd like to fill in the gaps. Certainly what's missing [from the proteomics data] is the membrane proteins," says Emili. Although similar resources exist for other model species, such as yeast, worm and fly, Emili acknowledges that bacteria have been largely understudied by genomics researchers. He hopes that this resource will help "bring in the bacterial community, making them aware of the things we can do with omics approaches."

Allison Doerr

RESEARCH PAPERS

Hu, P. *et al.* Global functional atlas of *Escherichia coli* encompassing previously uncharacterized proteins. *PLoS Biol.* **7**, e100096 (2009).

NEWS IN BRIEF

CHEMICAL BIOLOGY

Designing specificity

Designing molecules that specifically interact with only the intended biological target is a major challenge, especially in therapeutic applications. Grigoryan *et al.* describe a computational approach to design protein interaction specificity by maximizing the tradeoff between affinity and specificity. They used their approach to design highly selective peptide partners for 19 of 20 families of closely related human basic-region leucine zipper transcription factors.

Grigoryan, G. *et al. Nature* **458**, 859–864 (2009).

SENSORS

Fluorescent metabolite sensors

Brun *et al.* describe a general, modular approach for constructing fluorescence resonance energy transfer (FRET)-based metabolite-sensor proteins. The sensor consists of a Snap tag, a fluorescent protein, a metabolite-binding protein and a synthetic connector that contains both a fluorophore and a ligand that binds to the metabolite-binding protein. In the presence of a target metabolite, which displaces the connector ligand, the 'closed' sensor springs open and results in a change in the FRET efficiency.

Brun, M.A. *et al. J. Am. Chem. Soc.* **131**, 5873–5884 (2009).

GENOMICS

Identifying protein folding genes

Jonikas *et al.* describe a strategy to identify *Saccharomyces cerevisiae* genes involved in protein folding. They harnessed the transcription factor Hac1p, which activates the unfolded protein response, to drive expression of a GFP reporter. They introduced the reporter into ~4,500 deletion mutant strains and used flow cytometry to monitor single-cell fluorescence, thus identifying genes that either up- or downregulated the expression of the unfolded protein response reporter.

Jonikas, M.C. *et al. Science* **323**, 1693–1697 (2009).

PROTEIN BIOCHEMISTRY

A function for GFP

GFP, a protein found in the humble jellyfish, *Aequorea victoria*, and its fluorescent protein cousins have had a major impact on biological imaging. However, the biological functions of fluorescent proteins are not well-understood. Bogdanov *et al.* now report that GFPs can act as light-induced electron donors for various electron acceptors and suggest that they may play a role in cellular processes such as light sensing.

Bogdanov, A.M. *et al. Nat. Chem. Biol.* advance online publication (26 April 2009).

NANOTECHNOLOGY

Monitoring enzyme activity in real time

Orosco *et al.* describe a two-layer porous silicon nanoreactor as a label-free tool to monitor protease activity. The upper layer contains large pores, which trap the protease. The smaller reaction products filter down into the lower layer, which contains smaller pores. This causes a change in optical reflectivity of the silicon nanoreactor, allowing enzyme kinetics to be quantitatively observed in real time.

Orosco, M.M. *et al. Nat. Nanotechnol.* **4**, 255–258 (2009).