of model protein sequences, the researchers tested whether bipartite tetracysteine display could be used to monitor intramolecular protein folding and intermolecular protein-protein dimerization *in vitro*. In testing a wide variety of different contexts, they found that "in some cases the proteins [modified for bipartite tetracysteine display] are better behaved than in other cases, but in no case yet have we flat-out failed," says Schepartz, suggesting that the steric requirements for FlAsH or ReAsH binding to the bipartite tetracysteine motif are not quite as stringent as one might think.

They also showed that they could distinguish well-folded and misfolded proteins. Proteins with destabilizing point mutations still formed complexes with FlAsH or ReAsH, but the fluorescence was much dimmer in comparison to well-folded proteins (**Fig. 1**). They have not observed the formation of nonspecific fluorescent complexes of proteins that would otherwise not interact, though Schepartz does clarify that they have not extensively tested for this. Notably, the researchers also showed that their method can be used to detect protein folding and protein-protein interactions in live mammalian cells.

Schepartz and her colleagues believe that bipartite tetracysteine display offers a useful small-molecule alternative to FRET for designing new post-translational modification or protein-protein interaction sensors. The method should also be compatible with other techniques such as electron microscopy and could be used in high-throughput screening applications, for example, to identify small molecules that either stabilize or disrupt protein dimerization.

The future for this method indeed looks very 'bright'.

Allison Doerr

RESEARCH PAPERS

Luedtke, N.W. *et al.* Surveying polypeptide and protein domain conformation and association with FlAsH and ReAsH. *Nat. Chem. Biol.* **3**, 779–784 (2007).

Du and colleagues found that, although infection with a control virus had no effect on tumor progression, genes could be transmitted to the tumor cells and dramatically influenced tumor behavior. For instance, expression of a dominant-negative E-cadherin (a cell adhesion molecule) in these tumors caused similar phenotypes as coexpression of T antigen and dominant-negative E-cadherin in these pancreatic islet tumors. Opportunely, the researchers used this system to characterize a previously unknown role of the anti-apoptotic protein Bcl-xL in the cytoskeletal rearrangements that affect metastasis.

This system works particularly well for tumors that have stereotyped progression. As Du explains, "knowing the timing of development of hyperplastic lesions is important for introducing these avian viruses" at the desired stage of tumorigenesis. Once these variables are known, however, "this method has the flexibility to deliver a combination of the avian viruses encoding different genes simultaneously or sequentially to study their interactions in tumorigenesis," she says. So using viruses to deliver genes may not just save money and time over traditional transgenic techniques, but also make it possible to manipulate tumors *in vivo* in unprecedented ways.

Katherine Stevens

RESEARCH PAPERS

Du, Y.-C.N. *et al.* Assessing tumor progression factors by somatic gene transfer into a mouse model: Bcl-xL promotes islet tumor cell invasion. *PLoS Biol.* **5**, e276 (2007).

NEWS IN BRIEF

GENE TRANSFER

Human *ROSA26* locus

The *ROSA26* locus in the genome of mouse embryonic stem cells is easy to target and expresses transgenes well. Irion *et al.* identified the human equivalent of the *ROSA26* locus on chromosome 3. They integrated various genes into that locus and followed the multilineage differentiation of the targeted cells. Their locus provides a safe landing spot for transgenes and makes worries about gene silencing or disruption of endogenous genes because of random integration a thing of the past.

Irion, S. *et al. Nat. Biotechnol.* **25**, 1477–1482 (2007).

IMMUNOCHEMISTRY

High-throughput antibodies

Antibodies are key reagents for the study of protein function. Schofield *et al.* now screen a phage display library to identify human monoclonal antibodies on an unprecedented scale. They identified antibodies to 72% of 404 antigen targets, with an average of 25 specific clones to each. As with all high-throughput efforts, quality control and validation are key elements of the work.

Schofield, D.J. *et al. Genome Biol.* **8**, R254 (2007).

STEM CELLS

Fingerprinting stem cells

Haematopoetic stem cells differentiate to give rise to all the cells in the blood. By performing global gene expression analysis on these cells and on their differentiated progeny, Chambers *et al.* identified molecular fingerprints for specific cell types and cell lineages in the blood. This resource will be useful for developing markers and for identifying regulators of differentiation and cell fate specification in haematopoesis.

Chambers, S.M. *et al. Cell Stem Cell* **1**, 578–591 (2007).

CHEMISTRY

Synthetic lectins

Lectins are highly specific carbohydrate receptors that are being increasingly applied as tools for carbohydrate detection. Ferrand *et al.* designed a synthetic lectin analog that can recognize the disaccharide cellobiose with very high affinity and specificity. As the analog is much smaller than natural lectins, this represents notable progress toward the design of synthetic carbohydrate receptors for practical use as sensors.

Ferrand, Y. *et al. Science* **318**, 619–622 (2007).

IMAGING AND VISUALIZATION

Single-molecule tracking by fours

The need to track single fluorescently labeled proteins in living cells has created a desire for three-dimensional single-particle tracking methods using low-level illumination. Lessard *et al.* show that they can track single quantum dots using only 10 μW of energy by using four optical fibers coupled to individual detectors to effectively create four confocal pinholes that provide location information for feedback control–based tracking.

Lessard, G.A. *et al. Appl. Phys. Lett.* **91**, 224106 (2007).