therapy. "You can treat a disease at multiple different levels," he says. "You can have domains that inhibit proteins necessary for extravasation and domains that induce killing of the tumor cell." Although the cure for cancer with avimer therapy is not yet around the corner, their application to the clinic is not far off, and Stemmer is confident that clinical trials will begin next year on the use of their interleukin-6 avimer to treat autoimmune diseases.

One requirement for the clinical application of a molecule is low immunogenicity, a requirement the avimers fulfill, partly owing to their small size and partly because of a large number of disulfides. Work with other high-disulfide density proteins has shown that such proteins yield low immune responses, most likely because the presence of disulfide bonds makes the protein hard to cleave by intracellular proteases in antigen presenting cells. This cleavage is a prerequisite to the presentation of the peptides on the surface of these cells, which in turn triggers an immune response.

Another requirement for clinical application is the ability to manufacture the drug. Stemmer presents data showing the efficient production of avimers in bacteria, which should greatly reduce the cost of manufacturing relative to that for antibodies. In addition, the multiple disulfide bonds contribute to a high-temperature and stress stability, which may lead to longer drug shelf lives, and simplify the shipping and storage processes.

With their high target affinity, specificity and low immunogenicity, avimers appear to be well positioned for their first appearance in the clinic.

**Nicole Rusk**

**RESEARCH PAPERS**

Silverman, J. *et al.* Multivalent avimer proteins evolved by exon shuffling of a family of human receptor domains. *Nat. Biotechnol.* **23**, 1556–1561 (2005).



long-term responses, where long-term is like two days after you turn on the pathway." This system, on the other hand, allows rapid and dosage-dependent gene activation, allowing studies with far shorter time scales. Working with chimeric animals—with genetically modified cells positioned at different locations within the wing disc—Irvine and Ragulja were able to manipulate DPP-response gradients and immediately observe the impact on cell growth in different regions. The data suggested that the essential factor for cell growth is not the concentration of DPP, but rather the slope of the gradient, with growth resulting where neighboring cells show markedly different levels of DPP activity.

Irvine's group is now applying the same system to other gradient-dependent molecules, but Irvine adds that there has also been considerable interest from other groups looking to achieve equally sensitive modulation for their own genes of interest. "There's a number of different systems where it's nice to add this element of temporal control," he says, "and this is a pretty simple way to do it."

**Michael Eisenstein**

**RESEARCH PAPERS**

Rogulja, D. & Irvine, K.D. Regulation of cell proliferation by a morphogen gradient. *Cell* **123**, 449–461 (2005).

## NEWS IN BRIEF

GENE REGULATION

### Artificial cell-cell communication in yeast *Saccharomyces cerevisiae* using signaling elements from *Arabidopsis thaliana*

After constructing two hybrid strains of yeast—a 'sender' strain that expresses and secretes a plant-derived hormone, and a 'receiver' strain that expresses a hybrid signal transduction pathway capable of responding to the hormone—Chen & Weiss demonstrate the engineering of simple, synthetic networks that can model a variety of cell-cell communication processes.

Chen, M.-T. & Weiss, R. *Nat. Biotechnol.* **23**, 1551–1555 (2005).

PROTEOMICS

### Quantitative analysis of protein phosphorylation in mouse brain by hypothesis-driven multistage mass spectrometry

The sensitive detection of site-specific *in vivo* phosphorylation changes for a given target protein can pose a complex problem. Jin *et al.* offer a promising new solution, in which protein samples from drug-treated animals are subjected to a mass spectrometry strategy that allows simultaneous measurement of phosphorylation at many different residues, even at low levels.

Jin, M. *et al. Anal. Chem.*; published online 9 November 2005.

CELL BIOLOGY

### Unmodified cadmium telluride quantum dots induce reactive oxygen species formation leading to multiple organelle damage and cell death

It has been known for some time that quantum dots alone are cytototoxic and require modification for *in vivo* use. Lovrić *et al.* find that cells treated with 'naked' quantum dots undergo nonclassical apoptosis, exhibiting organelle damage and elevated generation of reactive oxygen species, and they suggest that the gradual loss of surface modifications may lead to *in vivo* toxicity.

Lovrić, J. *et al. Chem. Biol.* **12**, 1227–1234 (2005).

BIOINFORMATICS

### Kernel-based machine learning protocol for predicting DNA-binding proteins

Bhardwaj *et al.* describe a support vector machine (SVM)-based computational method for the characterization of DNA-binding proteins. After training their system for the analysis of features that distinguish DNA-binding from non–DNA-binding proteins, they are capable of achieving prediction with 85–90% accuracy without relying on homology or motif information.

Bhardwaj, N. *et al. Nucleic Acids Res.* **33**, 6486–6493 (2005).

IMAGING AND VISUALIZATION

### Light-switching excimer probes for rapid protein monitoring in complex biological fluids

Background signal can be an issue when using fluorescence for quantitative protein analysis. Yang *et al.* describe a modified aptamer whereby binding of target protein puts the molecule into an 'excimer' conformation that brings two pyrene molecules into close proximity, resulting in a fluorescence shift that is quantitative and can be easily distinguished from background.

Yang, C.J. *et al. Proc. Natl. Acad. Sci. USA* **102**, 17278–17283 (2005).