leagues took advantage of PS-CFP's preactivation fluorescence and stability at low pH to track the movement of tagged human dopamine transporter (hDAT) within filopodia (**Fig. 1**) and endosomes. They were also able to successfully photoactivate selected endosomes and track their movement in the cytoplasm. When two activated and nonactivated endosomes made contact, the authors observed, for the first time ever, the direct mutual exchange of cargo proteins between these cellular compartments, thus highlighting the value of PS-CFP for such studies.

As a further aid in localization and tracking, PS-CFP can be visualized with standard ECFP and FITC filters, making it straightforward to use in multilabel experiments with red fluorophores. A potential problem with PS-CFP is that unlike Kaede, which uses a different wavelength for photoactivation and visualization of the nonactivated form, PS-CFP uses the same wavelength at different intensities for both processes. PS-CFP is also slightly more sensitive to bleaching than EGFP, which could further complicate some experiments. However, the authors clearly demonstrate that as long as researchers are careful in their experiments, these drawbacks do not obviate the significant advantages afforded by this new addition to the photoactivatable fluorescent protein family.

Daniel Evanko

RESEARCH PAPERS

Chudakov, D.M. *et al.* Photoswitchable fluorescent label for protein tracking. *Nat. Biotechnol.* published online 17 October 2004 (doi:10.1038/nbt1025).

Patterson, G.H. & Lippincott-Schwartz, J. A photoactivatable GFP for selective photolabeling of proteins and cells. *Science* **297**, 1873–1877 (2002).

Chudakov, D.M. *et al.* Kindling fluorescent proteins for precise *in vivo* photolabeling. *Nat. Biotechnol.* **21**, 191–194 (2003).

Ando, R. *et al.* An optical marker based on the UV-induced green-to-red photoconversion of a fluorescent protein. *Proc. Natl. Acad. Sci. USA* **99**, 12651–12656.

binding sites, all showed strong inhibition; the strongest, BV3, with an IC_{50} 200-fold better than that of the monomeric ligand, contained a linker with an effective length of only 22 Å.

Fan's group believe that these ligands inhibit CT-ganglioside interaction partly through steric blocking, occupying a binding site while the unassociated ligand moiety physically interferes with further protein surface interactions. They are currently developing new assays, including cell-based systems, to further characterize this inhibition. Fan believes these findings could ultimately provide new directions for future drug design projects, as bivalent ligands appear to offer a simplified strategy for improving inhibition and ultimately "it's probably much easier to make large quantities of bivalent compound rather than the heavily designed, generally hard-to-make multivalent ligand."

Michael Eisenstein

RESEARCH PAPERS

Pickens, J.C. *et al.* Nonspanning bivalent ligands as improved surface receptor binding inhibitors of the cholera toxin B pentamer. *Chem. Biol.* **11**, 1205–1215 (2004).

Fan, E. *et al.* High-affinity pentavalent ligands of *Escherichia coli* heat-labile enterotoxin by modular structure-based design. *J. Am. Chem. Soc.* **122**, 2663–2664 (2000).

Zhang, Z. *et al.* Solution and crystallographic studies of branched multivalent ligands that inhibit the receptor-binding of cholera toxin. *J. Am. Chem. Soc.* **124**, 12991–12998 (2002).

NEWS IN BRIEF

CHEMICAL BIOLOGY

LEAPT: Lectin-directed enzyme-activated prodrug therapy

Robinson *et al*. describe a glycosylation-based system for cell-specific activation of a prodrug compound. A nonmammalian enzyme, α-rhamnosidase, is artificially tagged with a carbohydrate that enables targeting to and internalization by cells of interest; following introduction of a similarly glycosylated, rhamnoside-capped prodrug, strong, tissue-specific enzymatic drug activation is observed.

Robinson, M.A. *et al. Proc. Natl. Acad. Sci. USA* **101**, 14527–14532 (2004).

BIOINFORMATICS

Textpresso: an ontology-based information retrieval and extraction system for biological literature

Müller *et al.* have devised a system for the analysis of text from the abstracts, titles and body of published articles, after which the data is organized ontologically according to established categories. This system, which the authors term Textpresso, makes it possible to conduct more productive and efficient literature searches.

Müller, H.-M. *et al. PLoS Biol.*, published online 21 September 2004.

GENE TRANSFER

Self-inactivating retroviral vectors with improved RNA processing

Self-inactivating (SIN) vectors offer a safer alternative to conventional retroviruses for gene delivery, but typically suffer from reduced titer and inefficiency of RNA processing. Kraunus *et al.* have developed a modified SIN vector incorporating a favorable intron that considerably improves transgene expression from the construct, and a viral regulatory element that strongly elevates the titer.

Kraunus, J., *et al. Gene Therapy*, published online 16 September 2004.

PROTEIN BIOCHEMISTRY

The site-specific incorporation of *p*-iodo-L-phenylalanine into proteins for structure determination

Using a directed-evolution strategy, Xie *et al.* generated an orthogonal, variant tyrosyl-tRNA synthetase capable of specifically directing the incorporation of the unnatural amino acid *p*-iodo-L-phenylalanine at the amber stop codon in *Escherichia coli*. Introduction of this residue into proteins is shown to improve the quality of structure determination via single wavelength anomalous dispersion (SAD) phasing.

Xie, J. *et al. Nat. Biotechnol.*, **22**, 1297–1301 (2004).

BIOINFORMATICS

Comparative homology agreement search: an effective combination of homology-search methods

Alam *et al.* introduce a tool called comparative homology agreement search (CHASE), which integrates five different sequence homology search methods to obtain a combined 'E value' confidence estimate for homology that surpasses the analytical performance of any of the individual algorythms.

Alam, I. *et al. Proc. Natl. Acad. Sci. USA* **101**, 13814–13819 (2004).