Using both simulations and experimental analysis with high-density SNP microarrays, Craig and his team show that it is possible to identify an individual in a mixture of hundreds to thousands of genomic samples, even when the DNA of the person in question is present only in trace amounts (as low as 0.1% of the total). Craig estimates that this may not be the limit of sensitivity. "My guess is it could go down to about one in ten thousand," he says.

In addition to the consequences it will have for forensic analyses, this demonstration has implications for how pooled genotype data will be shared in the future. To protect individual privacy, the US National Institutes of Health and other organizations have already removed aggregate genomic data from public access, instating approval processes for accessing these data, similar to those already in place for accessing individual-level data.

Craig suggests, however, that there is another side to this story. "I hope this will open up the conversation about data sharing," he says. "In my opinion, you really need to share individual-level data, since you lose a lot of power when you just share the aggregate information, and our work now shows that, even in aggregate data, the identity of participants is not completely masked. And I think it's better to work out how to do this responsibly now, when the amount of data is manageable, than in five or ten years."

Natalie de Souza

RESEARCH PAPERS

Homer, N. *et al.* Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. *PLoS Genet.* **4**, e1000167 (2008).

pastoris. This suggests that the mutations introduced into the D03 mutant likely confer an overall stability to the protein, resulting in more robust expression. They also purified sixfold more D03 than the wild-type NTR1 from *E. coli*, and the mutant was more thermally stable in detergent-solubilized form, which may promote its crystallization.

Although the researchers have so far only reported results for NTR1, they are currently working on additional mutagenesis of NTR1 as well as testing the generality of the method for other GPCRs. Plückthun notes that the FACS-based selection method is likely to be applicable for evolving better-expressing variants of any membrane receptor that can bind a fluorescent ligand.

They also have yet to test whether their method can streamline the bottlenecks in GPCR crystallization. If such an approach does turn out to be general for evolving more crystallizable variants, it could be extremely powerful and have a major impact on our understanding of GPCR biology. "The interesting part is to understand how the ligand binds, the exact atomic details, and what the differences between an agonist and an antagonist are," says Plückthun. "I just don't think it can really be extrapolated from one model. We have to have an experimental access to basically the whole family."

Allison Doerr

RESEARCH PAPERS

Sarkar, C.A. *et al.* Directed evolution of a G protein–coupled receptor for expression, stability, and binding selectivity. *Proc. Natl. Acad. Sci. USA* **105**, 14808–14813 (2008).

NEWS IN BRIEF

MOLECULAR LIBRARIES

Histone mutant libraries

It is well appreciated that the functions of core histones are largely controlled by combinatorial post-translational modifications, but individual amino acid residues are also important in regulating DNA-damage response, transcriptional activation and heterochromatin formation. Dai *et al.* describe a systematic yeast-based library of histone H3 and H4 mutants, which they used to explore the contribution of each individual residue to nucleosome function.

Dai, J. *et al. Cell* **134**, 1066–1078 (2008).

GENOMICS

Genomic analyses of tumors

To really understand cancer biology it is important to understand all of its genetic and genomic alterations. Several groups have launched large-scale, multidimensional efforts to analyze copy-number variations and gene expression in human glioblastomas and pancreatic cancer. All data of these global genomic analyses are freely accessible.

Jones, S. *et al. Science* **321**, 1801–1806 (2008).
Parsons, D.W. *et al. Science* **321**, 1807–1812 (2008).
The Cancer Genome Atlas Research Network. *Nature*, published online 4 September 2008.

CHEMICAL BIOLOGY

Chemical control of proteins in mice

Banaszynski *et al.* expanded a previously developed method to control protein function in cells. They express a protein of interest as a fusion to an unstable domain. The unstable fusion protein is targeted for degradation, but the presence of a stabilizing ligand protects the fusion protein from degradation, in a dose-dependent manner. By using a viral vector to deliver the fusion protein, they now show they can control protein function in living mice.

Banaszynski, L.A. *et al. Nat. Med.* **14**, 1123–1127 (2008).

STEM CELLS

iPS cells without viral integration

Reprogramming of somatic cells to yield induced pluripotent stem (iPS) cells has only been achieved so far using technology that requires viral integration into the host cell genome. This poses problems for the safety of the approach, particularly in a clinical setting. Stadtfeld *et al.* now show that transient expression of Oct4, Sox2, Klf4 and c-Myc from non-integrating adenoviral vectors can reprogram mouse somatic cells to pluripotency.

Stadtfeld, M. *et al. Science*, published online 25 September 2008.

PROTEIN BIOCHEMISTRY

Evolving streptavidin

The extremely strong interaction between streptavidin and biotin has been exploited for many applications. Levy and Ellington used *in vitro* compartmentalization–based directed evolution methods to generate streptavidin mutants that bind the biotin analog desthiobiotin with the same affinity as the wild-type enzyme but with a 50-fold slower off rate, which may facilitate new applications. The method should also be applicable for evolving other very high affinity protein-ligand interactions.

Levy, M. & Ellington, A.D. *Chem. Biol.* **15**, 979–989 (2008).