their legal father. Given this culture, there is no reason why only immigrants with a biological link should qualify for integration with their families in France. Furthermore, DNA testing of immigrants elsewhere has destroyed families by uncovering true biological relationships.

The scientists' case has enjoyed public and political support, and has embarrassed the government, which sought to defuse the controversy last week by postponing a final decision to 2009. The outcry has also thrown an overdue spotlight on issues surrounding such population databases — issues being tackled in Britain, which has the world's largest DNA fingerprint database. The National DNA Database contains samples of 4 million people or 6% of the population, and one in ten males. The Nuffield Council on Bioethics, in a landmark report this month, does a service by drawing attention to the dangers of proposals to expand the database (see http://tinyurl.com/2upt8x).

There is a widespread misperception, encouraged by governments and media success stories, that DNA evidence is infallible in clinching convictions or acquittals. The technology is sound, but errors or deliberate falsifications in sample taking and handling are not uncommon, and a match with a sample at the scene of a crime may amount to proof only that the person was present at some point.

Since 2003, DNA samples and fingerprints have been compulsorily taken from Britons arrested for criminal offences. But the government now proposes extending the database to include fingerprints and DNA from anyone arrested, even for minor offences such as dropping litter. And voices within the UK government and the judiciary have suggested that the entire population should be sampled. The US government, meanwhile, is proposing to extend its database to include DNA from anyone arrested by federal agents.

The Nuffield report is right to denounce the infringements on liberty and privacy represented by such extensions as being disproportionate to any possible benefits. Suspicion of involvement in a minor offence cannot justify taking a biological sample without consent. In the United States, the largest group likely to be affected is illegal immigrants — and there is no reason to suspect this group of being more likely to engage in serious crime.

DNA fingerprints themselves contain relatively little personal information, but the biological samples are open to misuse. Although supposedly limited to direct matching of individuals for crime cases, DNA data are already used for the much less scientifically robust practices of searching for family relatives of a crime's perpetrator, and to try to reduce possible suspects to ethnic groups.

History teaches us that it is a fallacy that only those without a clear conscience need fear a knock on the door at midnight. Governments' enthusiasm for DNA databases needs to be matched by commensurate statutory protection, transparency and oversight — and vigilance by citizens. ■

Toxic alert

A method of knocking out genes in mice needs more discrimination than many have recognized.

One of the most common ways to investigate the role of a gene in human physiology is to delete its equivalent from a mouse genome and to observe the effect. The use of one enzyme in particular, the recombinase 'Cre', has revolutionized the study of gene function in mice. The technique allows researchers to introduce mutations and gene deletions in a tissue or cell type at any stage.

Hundreds of studies using this technology have been published since it was introduced more than ten years ago, shedding light on areas such as important developmental processes and the role of numerous genes in, for example, the immune or nervous systems, or in various diseases.

Briefly, it works by introducing the target DNA sequence used by the Cre enzyme, known as a *loxP* site, to either end of the gene sequence in question. By subsequently introducing the Cre enzyme, the sequence is excised. Gene targeting can be regulated by controlling where Cre is expressed or activated.

But the technology is not without its pitfalls. A number of issues have been described in a recent overview (M. Schmidt-Supprian and K. Rajewsky *Nature Immunol.* **8,** 665–668; 2007). Readers, authors and editors alike need to be alert to one particular problem: the potential toxicity of Cre expression to cells.

The induction of cell death as a consequence of Cre activity, unrelated to the targeting of any specific gene, is thought to occur when Cre targets sites similar to *loxP* that are present in genomic DNA, thereby inducing mis-recombination and DNA damage. Most mice strains in which Cre is expressed seem to develop normally and do not show any overt signs of Cre toxicity, and it is somewhat unclear exactly under what conditions it arises. It has been suggested to result from long-term expression of high levels of the enzyme.

Regardless of the exact mechanism and circumstances, Cre toxicity is clearly a potential problem, yet in the view of some researchers it has been neglected or played down in the community. In fact, one study has systematically analysed studies using a particular Cre mouse strain and found that in more than half of the cases the appropriate control for potential Cre toxicity — the use of the same mice without the *loxP*-flanked target gene — was not included (J.-Y. Lee *et al. J. Biol. Chem.* **281,** 2649–2653; 2006). *Nature* is aware that it has in the past published papers in which such controls were lacking, although many will no doubt have been independently validated with other techniques at the time or subsequently.

It can be argued that potential toxicity due to Cre expression becomes pertinent only when the observed phenotype resulting from gene targeting involves cell death, but the complexity of biological processes probably warrants attention to the issue in all experiments. Researchers planning experiments should take into account the need for additional mice as controls. Editors at *Nature* will consider the issue and the appropriate controls with referees during the assessment of submitted papers.

No technology is without caveats, and — as the *Nature Immunology* article concludes — there will always be a degree of uncertainty with which researchers have to live. But in the interest of best scientific practice, everyone involved would be wise not to neglect the dangers and subtleties at play even in routine experiments. ■