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Of mice and mutagenesis

It might seem hard to believe, but there is growing concern within the mouse genetics community that it is running out of interesting mutations to study. In part this is a symptom of the recent successes in genetic mapping and cloning that have led to the characterization of many of the mutants created shortly after the Second World War. For example, of the approximately 4,870 mouse genes that have been mapped, more than 4,200 have been cloned. Consequently, scientists in the United Kingdom and the United States have been meeting of late to sketch out plans for generating a large new round of mouse mutants. Unlike the spontaneous mutants of the past, which tended to produce easily visible phenotypes such as skeletal malformations, the idea is that the new strains would be made available to members of the community, who could then screen for a variety of more subtle defects, including behavioural abnormalities.

Chemical methods for mutagenesis have been in place for decades. Ethylnitrosourea (ENU), which produces primarily point mutations, and chlorambucil (CHL), which induces deletions, are both capable of inducing mutations at a given locus at a frequency greater than 1 in 1,000, and both are still in use. For example, Maja Bucan's group reported last year that a screen of ENU-induced mutants revealed a hyperactive circling mutation called *Wheels* (*Genetics* **140**, 245-254; 1995). Unfortunately, the screening and maintenance costs associated with these procedures in mice are exorbitant when contemplated on a wider scale, and yet their value in other organisms is unquestioned. Christine Nusslein-Volhard earned a share of last year's Nobel Prize for her mutagenesis studies in *Drosophila*, and is now analysing hundreds of mutant strains of zebrafish created using ENU (*Curr. Biol.* **4**, 189-202; 1994). There are also several exciting genetic techniques available in mouse, including the Cre-*loxP* system for inducing chromosomal rearrangements (*Nature* **378**, 720-724; 1995) and radiation-induced deletions in embryonic stem cells, currently in use in John Schimenti's group at the Jackson Laboratory.

Although producing a new generation of mouse mutants is appealing in theory, the hurdle of funding remains. One obvious site for storing such mice would be the Jackson Laboratory, but a project of this scope requires other sources of financing. The recent successes in cloning the murine obesity related genes, *ob* and *db*, underscore the clinical as well as fundamental biological importance of mouse genetic discoveries. It is to be hoped that these ideas can be set into motion before too long.