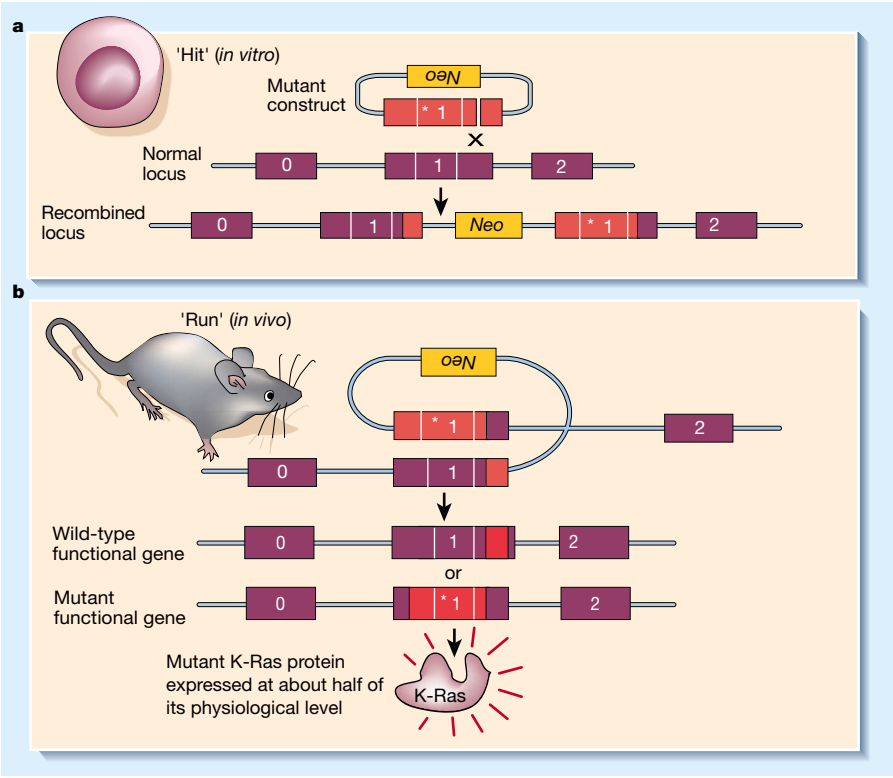

Figure 1 **A new 'hit-and-run' strategy for generating mouse models of sporadic cancers[4].** a, **A 'silent' mutant *K-ras* gene (oncogene) is inserted into the site (locus) of the authentic, normal *K-ras* gene in mouse embryonic stem cells, which are taken from early embryos. The insertion involves the mutant and normal DNA segments being shuffled (recombined). The altered stem cells are then used to generate mice. The asterisk represents the mutation. *Neo* is the neomycin gene, which allows cells that bear it to grow when cultured with the antibiotic neomycin. This enables researchers to identify cells that have taken up both this gene and the adjoining *K-ras* oncogene. 0, 1 and 2 represent the protein-coding sections of the *K-ras* gene.** b, **Within the mice, spontaneous recombination occurs either within or between chromosomes during cell division. Occasionally, this will result in the *Neo* gene being excised from the *K-ras* locus, producing a functional wild-type or mutant *K-ras* gene in random tissues. The active mutant K-Ras protein drives tumour growth.**

tumours. This could be because recombination frequencies are low in these tissues, or because different cells in different species respond differently to mutant *K-ras*. Indeed, cell-type-specific effects are almost certainly involved, as foci of early tumour cells in the animals' intestines did not become fully cancerous. Intriguingly, though, when the authors produced mice bearing both the *K-ras* oncogene and Apc^{min} — a mutated gene that predisposes humans to intestinal adenomas — the type and frequency of intestinal tumours did not change. One wonders whether the *K-ras* mutant was activated in tumours in these doubly mutant mice.

Jackson *et al.*'s mutant mice[4] represent a unique new model. Others, using different recombination techniques[9] to produce sporadic mutations, will no doubt follow suit. Sporadic activation of a recombination system *in vivo* has another advantage: it allows researchers to introduce several genetic alterations at a defined moment in a subset of cells, increasing the ability to mimic a wide spectrum of human tumours. These models should allow us to work out the sequence of events, including field cancerization, in tumour development. They also seem well suited for testing prevention strategies and treatments. A further practical refinement of these models will undoubtedly include sensitive *in vivo* imaging. For example, it might prove possible to activate luciferase, a light-generating enzyme, only in specific tumours — a promising way by which such features as tumour growth, spread, regression and relapse can be monitored non-invasively[10]. Expectations are high, but the proof of the pudding will be in the eating. ■

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Daedalus

New life

The British House of Lords has ruled that stem cells from fetuses can be used in medical research; nonetheless, we would all like a way of minimizing this source. Stem cells, of course, are only a few generations away from their creation. They express on their surface few or none of the histocompatibility molecules which bring the immune system down on them so heavily. Furthermore, the brain is a relatively privileged immunological site. That is why victims of Parkinson's disease, for example, can receive an injection of alien cells which will not be rejected. The cells may take their developmental cues from the brain around them, and reverse the effects of the disease.

So, says Daedalus, the best way forward would be to multiply stem cells *in vitro*, so that they could all be generated from just one fetus. DREADCO biochemists think that the medium is important. The best medium would be very 'young' — it should contain spinal fluid, and so forth, from very young organisms. It should be devoid of polarity cues, as this would encourage the cells to remain pluripotent and would repress any development or the establishment of gradients. A stirred system should do this.

So DREADCO biochemists are devising new media in which stem cells can be grown without deviating towards development. They are doping purely synthetic media with extremely young spinal fluid, brain fluid and so on, hoping that the cells will remain undeveloped for many generations. With luck these cells will be largely immune from immunological rejection. Thus in the brain they would take their developmental cues purely from the organ around them.

Indeed, says Daedalus, many simpler organisms, such as lizards, can regenerate legs or tails that become damaged or missing. They seem to be able to reverse cell development, and create new stem cells for the missing organs. With luck, plentiful human stem cells will enable humans to repair broken or missing arms and legs and wrecked tissues without the current trouble and limitations. All sorts of human damage could then be neatly repaired by allowing the cells to carry out the developmental plans which must be present even in the stump of a limb. Only the immune system, more active in the body than the brain, will have to controlled. And heart-transplant teams have already shown how to do this. **David Jones**