Fat (and thin) rats distort results

Sir — It was gratifying to see M. Festing[1] address one of the most vexing problems in toxicology, that of rodents so obese that the validity of carcinogenesis screening is brought into question[2,3].

Festing recommmended the use of isogenic rather than outbred strains of rat. But he did not mention some work that had already been done using isogenic strains. The problem in carcinogenicity screening tests of increasing tumour rates (in the anterior pituitary gland, for example) and decreasing survival, accompanied by an increase in body weight, was actually first reported in an isogenic strain, the F-344 rat[4].

We have related body weights to survival and neoplasia (such as leukaemia) in the same F-344 rat[5]. We[6] and others[7] have also correlated body weights to liver (and other) tumour incidences as well as increases in body weights to increases in tumour incidences over the same time period in another isogenic strain used in carcinogenicity tests, the B6C3F1 mouse. These studies have identified a major source of the variability in the tumour incidences of control animals used in carcinogenicity tests as the differences in body weights in the various studies.

Rather than incurring the problems that ensue from changing strains, or trying to breed small animals, one approach is to use dietary control[6], which maintains body weights at predetermined practical ranges through control of dietary intake.

This approach not only prevents the 'fat rat', but also minimizes the variability in tumour endpoints and survival associated with the usual wide range in body weight seen in toxicology studies. Control of this variability is important because, besides being too large, rodents can also be too small in carcinogenicity bioassays, because of either an inadvertent restriction of feed or exposure to an agent, and thus be fairly insensitive to the action of toxicants.

We strongly support the evaluation of new models in biological studies. However, new models require painstaking evaluation and comparison with those now accepted by the toxicological community so that their results can be put into a proper context. We have a wealth of results in the strains used in toxicity testing that allow the kinds of comparison necessary for the development of new procedures that can provide improved means to assess human risk.

The complicating effects of uncontrolled body weight in toxicity tests is a consequence of the practice, common in rodents although unusual for most test species, of *ad libitum* feeding.

These complications do not appear restricted to either isogenic or outbred strains, or only to certain rodent species. Indeed, they are not confined to carcinogenicity tests *per se*. The doses required to produce short-term toxicity vary two- to fourfold, based on the dietary intake and resulting body weight of the animal[8].

So dietary control could be a better solution than the genetic approach to resolve the problems currently observed in toxicity tests resulting from 'fat rats' and the other sequelae of uncontrolled food consumption and growth.

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Whodunnit?

Sir — A recent leading article detailed some of the difficulties involved in arbitrating authorship of scientific papers and concluded that attempts to define rules for authorship are "doomed to fail" (*Nature* **387,** 831; 1997). Although this is probably true, some of the thornier issues surrounding authorship could be mitigated if journals simply required the contribution of each author to be briefly stated. The rules the authors had applied in determining authorship would then at least be explicit.

For example, a paper (similar to that described in the leading article) on the discovery of a previously unknown hominid using a novel fossil detector might include the following statement: CM: fossil discovery, morphometry, principal author; PW: stratigraphy, assessed paper; MC: isotopic dating; LG: inventor of CRD (carbon replacement detector); PC: funding, intellectual contributions, co-authored paper.

Such a statement could be placed in the acknowledgements and would serve to allocate both credit and responsibility for the work being published. Such information, if generally available, would be widely useful in making hiring and tenure decisions, evaluating grant applications, judging published work submitted for doctoral theses, and, when necessary, determining responsibility for fraud.

Despite its utility, some investigators are likely to view this proposal as unnecessary, inconvenient or even demeaning. Journal editors will want to tread lightly so as not to alienate their contributors. Nevertheless, by taking the longer view (as you encourage authors to do), journals can serve the enterprise of science by helping authors to allocate credit fairly for their work and to accept responsibility for it.

Nature's pre-eminent position among journals of science gives it a unique opportunity in this respect. Few prospective contributors, I suspect, would forgo the opportunity of publishing in *Nature* simply because they were required to state their respective contributions.

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Nepotism and sexism in peer-review

Sir — I and my colleagues read with interest the Commentary by Christine Wennerås and Agnes Wold about nepotism and sexism in peer-review in the Swedish Medical Research Council (*Nature* **387**, 341–343; 1997).

We keep under constant review the fairness of our peer-review procedures and seek to ensure that our boards, committees and panels are constituted to reflect the clinical, non-clinical, gender, age, ethnic origin and geographical spread of the biomedical community in the United Kingdom.

But although our own data (which are available on request) do not suggest *prima facie* evidence of bias, the Swedish study has prompted us to carry out a review of the outcomes of our competitions so that we can be sure we have done all we can to eliminate bias.

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