

there is very little on DNA modelling. Some discussion on the contribution of Graphics to research in Molecular Modelling would be useful.

Molecular Graphics is a rapidly growing area which will benefit as hardware costs continue to fall. This will make the technology more accessible. This collection of abstracts, however, is aimed mainly at those already working in this field and will have limited appeal outside it.

FRANK WRIGHT

*Institute of Animal Genetics
University of Edinburgh*

Environmental Health Criteria 51: Guide to Short-Term Tests for Detecting Mutagenic and Carcinogenic Chemicals. W.H.O. 1985. 208 pages, Sw. Fr. 15, ISBN 92 4 15 41911.

The stated objective of this conveniently sized and priced book is to represent the views of the International Commission for Protection Against Environmental Mutagens and Carcinogens (ICPEMC) on the guidance which should be given in the field of short-term testing for mutagens and carcinogens with genetic activity. It is also stated that 'developing countries' '... provide the *raison d'être* of the present document, which is offered in a spirit of helpfulness in the hope that it may enable short-term genotoxicity tests to be used in a reasonable manner' (p. 12).

All contributors are European, six from the United Kingdom and three from West Germany (one now working in The Netherlands). None has worked for any significant time, if at all, in a developing country. This omission from the experience of the contributors should not be underrated, although it is understandable since so few people working in genetic toxicology have had the privilege to visit, let alone work in, a developing country. In fairness, this reviewer has none of this experience either.

The value of this book lies in its succinct, uncomplicated summary of many aspects of genetic toxicology and moderate resistance to the temptation to overrate its status. Thus, '... any assessment of test results in terms of mutagenic or genotoxic hazard can be properly made only in the context of the whole toxicological profile of a substance and its use' (p. 12). As a summary and introduction to methods used in developed countries, this book is valuable and should legitimately find a market among the many practicing technologists in the field. It will also be useful to people in developing countries with an interest in environmental health, if only so they can be informed about lines of thought currently followed in their industrialized neighbours in a rapidly shrinking and complex world.

But – there had to be one – certain practicalities have been overlooked if this is intended to be a manual from which protocols may be written and used in developing countries. Why include a description of a

dominant lethal assay? This is not cheap (a rat assay can cost £20000), uses large numbers of animals (say, 100 male rats or mice and 1600–2000 females from which 20000–30000 fetuses are killed) and provides very limited information. Such carnage needs better justification than is currently given for a dominant lethal assay on scientific grounds. Scientists and technicians alike do not – in my experience – relish dominant lethal assays and would rather not do them. Transpose these misgivings to a developing country and the rejection of this assay for widespread usage is a foregone conclusion.

Any mammalian cell mutation assay is going to be extremely difficult to conduct in a developing country, not only because of problems in justifying the expenditure on specialized equipment, but also because most of these countries are both hot and wet: delightful conditions for yeast and fungal growth, so establishing the opportunity for contamination of culture medium and leading to yet more expense as experiments are lost.

A different reason for detraction from the stated objective of the book is the prioritization process. Far be it from the likes of me to tell a developing country how its resources should be spent, but the local major problems requiring solution are likely to be identified already, at least in general terms. What remains is education, control and chemical analysis. It is known that burning any organic material generates mutagens, carcinogens, promoters, etc. It is known that fungal contamination of food is likely to leave that food tainted with toxins. It is known – or should be – what the toxic hazards are for chemicals first synthesized elsewhere and now being either imported or manufactured within the developing country.

A major problem in many countries is not establishing whether some esoteric chemical induces mutations in bacteria, but in reducing the concentrations of lead, mercury and cadmium in water from levels that in any industrialised nation would be totally unacceptable and considered highly dangerous. What is required is digestible information, as was pleaded for recently by Professor Darmansjah of Indonesia at the IV International Congress of Toxicology. In his country clothing dyestuffs may be used as food colours, mercury is used in spot removal cosmetics and is present at high levels in 'edible' fish, and there are around 500 hospital admissions each year for pesticide poisoning treatment. Such problems of control and the implementation of action based on currently available information extends to the pharmaceutical industry also (Richards, *BMJ* (1986), 292, 1347–1348). The need is not for new information, at least not from short-term tests, but a knowledge of what to do with it. Having tempted these nations out of an equilibrium slowly changing over centuries and into the hurly-burly of a consumer society, we owe them the knowledge of how to deal with the hazards.

Some space is given to the selection, application and

interpretation of short-term tests. The use of at least two tests is advocated: a bacterial mutation assay and either an *in vitro* or an *in vivo* chromosome assay. The two *in vitro* tests are commonly used, 'Because they performed well in validation studies and currently have a good predictive value for animal carcinogenicity with many classes of chemicals' (p. 156). This is a contentious statement. Firstly, it has been easily demonstrated that 'predictive value' [if a chemical is positive (or negative) in the short-term test, what is the probability that it will be a carcinogen (or non-carcinogen)?] is an invalid and misleading concept (Cooper *et al.* *Br. J. Cancer* (1979), **39**, 87–89).

Secondly, the sensitivities and specificities, even for the better of the two assays (the bacterial mutation test), have fluctuated wildly in different studies (Brusick, *Ann. N. Y. Acad. Sci.* (1983), **407**, 164–176), so, to say these assays have performed well ignores some real problems. Thirdly, if one needs to err on the side of safety (given the fallibility of all current assays) then it might be argued that a mouse lymphoma mutation assay should be used in place of the *in vitro* cytogenetics test because more carcinogens are positive in the mouse lymphoma assay than in the latter.

Currently, most *in vitro* assays give many positive responses with the so-called non-carcinogens, perhaps because it is against the rodent carcinogenicity tests that the performances of *in vitro* tests are being measured. Mouse and rat respond to the same carcinogens only about 70% of the time, so how can we place our confidence in correlations between a *relatively* simple process – mutation – and rat and mouse carcinogenicity? And where does man fit into this scheme, which regulators have come to accept under sustained pressure from scientists? We should consider whether we are using these short-term tests correctly. If genotoxic activity is truly demonstrated, then perhaps that is how it should be accepted. This activity may be part of the mechanism through which a chemical is toxic in an animal, and man may or may not be such an animal. It appears to this reviewer that any response (significant or not) in a genotoxicity test should be investigated in an effort to show what the result means for man. The adjective, 'short-term', should not be applied to these tests any more than it is applied to the measurement of, say, pH; they describe certain properties of a compound which may be relevant in the assessment of the toxicity of a compound to man. Mostly, the genotoxicity assays allow data accumulation in a short time. The time has come to slow down the testing and consider what the data mean.

While this sentiment has not been stated in such undiplomatic terms in the book, it is partly shared by its authors: 'Evidence from *in vivo* mutation studies, pharmacokinetic data, or long-term animal studies may, however, remove the concern caused by an isolated positive result in an *in vitro* assay' (p. 168).

But how often are *in vivo* mutation studies performed? Are we expecting too much from pharmacokinetics? Can we trust long-term animal studies as being predictive for man? Are the best interests of mankind served by technically accurate books such as this one, but in which very real problems are hardly addressed?

D. B. MCGREGOR

Inveresk Research International Limited
Musselburgh EH21 7UB
Scotland

Molecular Genetics of Filamentous Fungi. Edited by W. E. Timberlake, UCLA Symposium on Molecular and Cellular Biology, vol. 34 465 pages, N. Y.: A. R. Liss Inc. £57.00. ISBN 0 8451 2633 4.

This book contains the proceedings of a symposium held at Keystone, Colorado in April 1985 and is divided into 7 sections totalling 32 articles one of which is simply an abstract. As is usual in proceedings of this type the articles are a mixture of reports of comparatively recent research on specific topics and more broadly based reviews.

If there is one area on which the advances in filamentous fungi have trailed behind those in yeast it is in the development of systems of efficient transformation and directed mutagenesis. Recently there has been considerable progress in remedying this deficiency and the first section contains six chapters recounting developments in this area. Other sections are concerned with metabolic regulation (7 chapters and one abstract), differentiation and development (3 chapters), the cytoskeleton (4 chapters), genome organization and evolution (5 chapters), industrial fungi (2 chapters) and fungal pathogenicity (4 chapters). Attempts to improve transformation techniques also feature in these other sections. I found the section on the molecular genetics of the cytoskeleton, in which the chapters by Oakley and May *et al.* are noteworthy, and the section on the molecular basis of fungal pathogenicity of particular interest.

The section on 'Genome Organisation and Evolution' is also both informative and interesting. Russel *et al.* report on their investigations into DNA methylation in *Neurospora*. The low level of methylation present in most fungi makes analysis difficult but, of course, the low level does not preclude a biological significance. Methylation in *Neurospora* was investigated using stable isotope gas chromatography – mass spectrometry which allows the detection of much lower levels of methylation than HPLC. The detection of differing methylation patterns in rDNA from conidia and mycelium suggest that they could be important and warrant further investigation. Metzberg *et al.* report on the existence of several isotopes of 5S RNA in *Neurospora* which are maintained as major and minor variants across species and genera. The genes encoding each of these isotopes are found as multiple copies scattered across the genome. The