

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

problem of how a scattered family of isotypes is maintained as a homogeneous set is one which is considered at length. The authors conclude that RNA-mediated gene conversion is the likely mechanism.

In edited works, unlike books of single authorship, the value of the whole is rarely greater than the sum of the individual parts. The valuation put on individual chapters will no doubt vary from reader to reader; as far as this reader is concerned there were enough stimulating chapters to maintain my interest throughout. I did, however, encounter minor points of irritation. Not all the authors cite their references in the same way, whilst references in most chapters are cited in full, in others the titles are omitted, a method of reference citation which I personally find annoying. Another example of the autonomous non-integrated nature of the contributions is, perhaps, more important. The report of the conference is incomplete in that not all participants submitted manuscripts for publication. The editor explains in his introduction that 'some speakers felt the information they presented was not appropriate for a proceedings volume'. In a review of differentiation and development, Lovett refers to the interesting talk of Champe on conidiation mutants of *Aspergillus* and the light which they throw on competence of the organism to respond to induction signals. Unfortunately an account of Champe's talk is not to be found in the proceedings, an omission which leaves the reader frustrated and with the distinct feeling of having missed out on something.

In a rapidly developing area like the one dealt with here, libraries have to purchase new books if they are to stay up to date; on the other hand a book's useful half life is limited as the reports it contains are overtaken by further developments. In the present financial climate when expenditure on educational matters is severely restricted, a decision to purchase books in a rapidly evolving field is therefore a fine judgement. In the final analysis the balance falls decisively in favour of recommending this book to all libraries with an interest in this area.

JEFF BOND

*Department of Genetics
University of Edinburgh*

Lysosomal Storage Diseases. Biochemical and Clinical Aspects. By RICHARD W. E. WATTS and DOROTHY A. GIBBS. London: Taylor & Francis, 1968, 284 pages, £35, ISBN 0 85066 326 1.

This book reviews the thirty or so inherited metabolic disorders that give rise pathologically to lysosomal storage in man. These diseases are of interest not only because they account for some 15% of known metabolic diseases but also because they have often been at the forefront of new developments such as prenatal diagnosis, enzyme replacement therapy and

cdNA cloning. Many of these aspects are in fact covered in this book.

The eleven chapters deal with the following subjects: biochemical diagnosis, genetics, sphingolipidoses, mucopolysaccharidoses, glycoproteinosis, mucopolipidoses, acid lipase deficiencies, glycogenosis type II, approaches to treatment and future prospects. Sections dealing with specific diseases are subdivided into: biochemistry, clinical phenotype, pathology, biochemical diagnosis and genetics. Most disorders are covered but the omission of cystinosis is more than a little surprising since this disease is not uncommon (sixty-six patients were reported in one French study) and the disease has been known since early this century. Recent reports suggest that the accumulation of cystine results from a defect in a specific ATP-dependent transporter across the lysosomal membrane. A similar defect may account for the accumulation of sialic acid in Salla disease, which is discussed but may not be confined to Finland as suggested. Cases have now been found in North America, Belgium and the U.K. On the subject of diseases covered, I was disappointed to find lactosylceramidosis appearing again. Subsequent biochemical and neuropathological studies have shown that the original patient almost certainly had the type C variant of Niemann–Pick disease (where lactosylceramide as well as other lipids commonly accumulate).

A number of other irritating errors have crept into this book which for me, I am afraid, devalued what would otherwise have been an excellent account, being both well written and clearly laid out. Useful tables and figures abound many of which have been taken from well-recognized and standard works but some of these, such as the illustrations of patients with type A Niemann–Pick disease and Farber disease, should surely have been properly acknowledged!

In discussing approaches to prenatal diagnosis the authors rightly point to the unknown risks of spontaneous abortion following chorionic villus sampling, however the most recent survey reported is protected by anonymity! An informative table is provided giving a choice of samples recommended for enzyme diagnosis. But I wonder how much experience the authors have had of diagnosis of Krabbe disease with serum or Pompe disease with leucocytes; each would require special care. Similarly the removal of neutral β -galactosidase is not normally necessary when diagnosing GM1 gangliosidosis, and serum or urine should certainly not be used.

In the chapter dealing with the mucopolysaccharidoses the authors are obviously more on home ground and a much better account is given. There is an excellent review of glycosaminoglycan structure and degradation and both Hurler and Hunter diseases are particularly well covered. On the other hand, Sanfilippo disease, which may be equally common and exists in at least four enzymatic variants, was given rather short shrift. When discussing the X-linked