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BOOK REVIEWS

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Molecular Genetics of Nervous System Tumours. Ed Arnold J Levine, Henry H Schmidek. (Pp 426.) New York: Wiley-Liss. 1994.

When I agreed to review this book I anticipated, somewhat naively, that I would receive a rather slender volume. I was rather startled when a large tome weighing 1.5 kg arrived. A quick inspection of the contents pages showed not that there had been a sudden and vast increase in knowledge about the molecular genetics of nervous system tumours, but that the editors had chosen to include a fairly wide ranging selection of reviews on nervous system development, oncogenes and growth factors, effective ionising radiation on the central nervous system, and strategies for gene mapping and isolation. Together these sections comprise nearly half of the book. The latter half of the book is devoted to reviews of cytogenetic analysis of human brain tumours and molecular genetic analysis of nervous system tumours. The final sections in the book are devoted to metastatic disease within the nervous system and reviews of experimental brain tumour therapy based on viral vectors or plasmids expressing anti-sense transcripts.

Coedited by a scientist and a neurosurgeon, the book is aimed at both scientific and clinical audiences. Most scientists working on the genetics of human cancers will find that substantial parts of the book deal with subjects already well known to them. However, those of them who are unfamiliar with work on nervous system tumours will find the latter half of the book to be of interest. The majority of clinicians whether they be oncologists, radiotherapists, or neurosurgeons will probably be unfamiliar with most of the subjects covered. On balance I would expect this book to be read rather more by the clinical than scientific fraternity.

As a Paediatric Oncologist I turned first to the chapters on cytogenetic analysis of paediatric brain tumours and molecular genetic analysis of medulloblastomas. My prejudice that little progress had yet been made in understanding the genetic basis of paediatric brain tumours was reinforced. There was little information on genetic mechanisms compared with the extensive knowledge that has been gleaned over the past 10 years for other paediatric solid tumours. Review of other chapters indicated much of the same problem. The sections that I found most interesting were those devoted to metastasis within the

central nervous system and experimental therapies for brain tumours.

Although this book is a brave attempt to provide a definitive review of its subject, it is a little disappointing because of the lack of progress thus far in the subjects addressed. It is, though, well written and in places quite stimulating. A second edition incorporating the most up to date advances in, say, three years time would probably be a very exciting volume. Who should read this book? Ideally they would have a postdoctoral level of scientific knowledge and have a particular interest in nervous system tumours. Thus a postdoctoral scientist beginning work on a relevant project or an oncologist or neurosurgeon with some scientific background would probably find a number of chapters to be worthwhile. I doubt that many people in Britain would buy a personal copy but it is probably worth larger neuroscience departments having a copy.

CHRISTOPHER MITCHELL

Gene Targeting: A Practical Approach. Ed A L Joyner. Practical Approach Series Editors D Rickwood, B D Hames. (£19.50.) Oxford: IRL Press at Oxford University Press. 1994.

Gene targeting offers a powerful technique for the study of gene expression and mutation and models of human genetic disorders created with such technology have abounded over the last few years. While most people are familiar with the overall theory, the actual mechanics of ES cell culture, blastocyst manipulation, and mouse work are less well known, often presented as shortened summaries in the materials and methods sections of papers. This has led to the protocols by which successful targeting is achieved being guarded and passed around by word of mouth or fax. To counteract this, this book brings gene targeting into the open.

We are all aware of the Practical Approach Series from IRL Press and many laboratories are adorned with their familiar cover layout. They give practical information to researchers starting out in a field and provide the basics in a solidly practical layout. In *Gene Targeting*, individual chapters from specialist authors are welded to a common theme with detailed protocols from the maintenance and manipulation of ES cell lines through to the details of animal husbandry and the surgical manipulations required to reintroduce blastocysts. Researchers familiar with this area should not lose heart, as sections in this broad reaching book make it an excellent reference to recent developments in transgenic technologies and gene targeting.

The book opens with a lengthy section on the molecular biology behind the vectors that can be used for targeting. The theoretical and practical considerations of replacement and insertion targeting vectors and the modifications needed to maximise targeting frequency are discussed in great detail. The chapter ends with an excellent discussion of making more subtle mutations including "Hit and Run" systems. This is essential reading for those embarking on such projects, and is suitably placed as the opening chapter.

In chapter 2, we get to grips with the propagation and manipulation of ES cell lines. Photographs of ES cell and colony morphology, which is essential to monitor to en-

sure that differentiation does not occur before reimplantation, make a useful inclusion. Detailed protocols include those needed for the production and maintenance of feeder cells, even the density at which to plate cells in culture to ensure successful growth. Electroporation, screening for homologous recombination events, DNA preparations, and the freezing down of large numbers of lines are all covered in practical protocols.

Chapter 3 represents a departure from the use of ES cells: the use of bone marrow stem cells for gene targeting. This is not commonly used, but warrants a chapter as it may be the technology of the future: the correction of gene defects in cell lines and the manipulation of tissue explants.

In chapter 4, we come to the beginning of two chapters on the mouse work needed to produce chimeric mice. To most people, this is probably the least familiar aspect of this area of research. The surgical methods and animal husbandry are covered in great detail, with photographs to carry you through the detailed manipulation and reintroduction of blastocysts. In contrast to the preceding chapter, which aims at making chimeras through the injection of ES cells into blastocysts, chapter 5 presents a less commonly used technique of ES cell aggregation to form blastocysts. This has the advantage over the injection of ES cells in that the mice produced are completely ES cell derived. This is expected to give a completely transgenic animal in the first generation, rather than relying upon chance germline transmission.

The book concludes with a chapter on the use of ES cells with enhancer and gene trap screens where specialised vectors, frequently carrying a lacZ reporter gene, are inserted randomly and the mice generated studied for a phenotype and assayed for gene expression. It contains an exhaustive list of constructs which have been made and published, an important starting point for anyone considering starting out with such a strategy.

As has become the norm for this series of publications, this book lives up to the practical approach title. For experimental detail the layout is excellent. It very much brings this technology into the open, and against the several other rival publications in this rapidly moving area, it stands its ground well.

MARK HIRST

Molecular Genetic Medicine. Volume 3. Ed T Friedmann. (Pp 184.) New York: Academic Press. 1993.

As previously discussed in these columns, the success of detailed review articles depends on a combination of good timing and originality. The best subjects are often those that require the drawing together of various disparate threads, rather than simple linear thinking. Unfortunately, this third volume of *Molecular Genetic Medicine* is probably the least successful to date, because most of the six articles fail to meet one or both criteria.

Two contributions are simply out of date. "Molecular biology of Alzheimer's disease" (Whitehouse, Landreth, and Younkin) focuses largely on the biology of neurotrophins and β amyloid precursor protein. Although it provides a good, scholarly treatment of these topics, there are virtually no references of 1992 or 1993 vintage. Thus no mention (or

even premonition) is made of the association of Alzheimer's disease with the apoE e4 genotype, a finding that has set the field alight. As for "Hunting for Huntington's disease" (Gusella and MacDonald), events over the past year have progressed so rapidly (in large part, it must be said, through the authors' own efforts) that the chapter is of little more than historical interest. The article by T Friedmann "Milestones and events in the early development of human gene therapy" is a somewhat longer rehash of a recent review by the same author in *Nature Genetics*, and this subject has been well chronicled by others too.

Of the other three articles, it is good to see cancer making its first appearance in the series, given the remarkable contribution of molecular biology to its understanding. "Genetics of astrocytic tumor progression" (Mikkelsen) provides a reasonable overall introduction, but analysis of the particular tumour chosen seems to be several steps behind colon cancer, so that it does not provide an ideal illustrative model.

Probably the most successful chapter is "Molecular biology of cystic fibrosis" (Drumm and Collins). After the frenzy of activity during and after the cloning of the CFTR gene in 1989 (well described here), it is a good time to take stock as the first trials of cystic fibrosis gene therapy get under way. What is most surprising is how much remains to be understood about the basic pathophysiology of cystic fibrosis. What are the regulatory elements controlling expression of the CFTR gene? Which CFTR mutations give rise to unstable mRNA and which to abnormal proteins? Which mutant proteins are transported to the plasma membrane and which fail to reach it? It seems that (at least in 1992!) the answers to these questions, so crucial to the design of rational therapy, were still far from clear.

The proper emphasis on ethical issues continues with "Genetics, insurance, and the ethics of genetic counselling" (Rothstein). This subject was largely ignored until a couple of years ago but is now the subject of a growing bibliography. This article is certainly worth reading, although because it concentrates on the issues from a USA perspective, not all of it will apply in other countries.

ANDREW WILKIE

The Genetic Basis of Common Diseases. Ed R A King, J I Rotter, A G Motulsky. (Pp 978.) Oxford: Oxford University Press. 1993.

This valuable book is a landmark for the specialty of Medical Genetics, perhaps equi-

valent to *Mendelian inheritance in man* or *Metabolic basis of inherited disease* in its breadth and detail. Its importance is not because the topic itself is new – chapters on genetics of common disease have appeared over the years in various system orientated books and as reviews – but because this represents the first attempt to provide a definitive overall account of the genetic contribution to common diseases in general. Its very existence is a statement that genetics as a scientific discipline, and medical genetics as a clinical specialty, stand in the mainstream of medicine and cannot be relegated to the area of rare (and thus by implication less important) conditions.

Ten years ago this book could not have been written or, if it had, it would have been of limited value. What has changed the situation is, of course, the emergence of molecular genetics and the identification of specific genes involved in an abundance of different diseases. Until recently, these advances had their impact principally on mendelian disorders but now the focus is shifting rapidly to the role of specific cloned genes in the pathogenesis of and susceptibility to common diseases. It is probably true to say that most of the relevant research is now going on in departments other than those of Medical or Human Genetics, but the fact that the techniques and approaches owe so much to the earlier work on mendelian molecular genetics has made the links between Medical Genetics and other clinical specialties closer than ever before.

It is difficult in a work of this scope to single out chapters for individual mention; there is a uniformly high standard, with most authors being leaders in their specific fields. Diabetes, coronary heart disease, and the major psychoses are key subjects which are all covered clearly and in depth, but so are most systems. The introductory chapters provide a valuable foundation, especially for the non-geneticist.

This work is an essential companion for anyone involved in medical genetics as a clinician, while laboratory scientists will find it extremely helpful in filling out the picture of their research area, as will clinical specialists in the different disorder groups. The editors and authors are to be congratulated on bringing such an important book to fruition. They should already be giving thought as to how best to keep it updated in the face of the explosion of information that is appearing, and that will make regular renewal essential. The publishers will similarly need to use all the means possible to help them in this. Meanwhile, they can all feel justly satisfied with the book that they have created.

PETER S HARPER

NOTICES

Fifth European Neurofibromatosis Group Meeting

The Fifth European Neurofibromatosis Group Meeting will take place in Leuven, Belgium on 6–8 April 1995. Enquiries and further information: Dr Eric Legius, Centre for Human Genetics, Herestraat 49, 3000 Leuven, Belgium. Tel: (32) 16 345903; Fax: (32) 16 346051.

International Symposium on Genomic Imprinting

An International Symposium on Genomic Imprinting will take place at Palazzo dei Congressi, Florence, Italy on 20–22 November 1994. Further details from the Organising Secretariat, Human Genetics Service, Department of Paediatrics, University of Florence, 209 via Masaccio, 50132 Florence, Italy. Tel: (39) (55) 5662931/941; Fax: (39) (55) 570380.

EUROMEDECINE 94

The 10th International Medical and Pharmaceutical Research and Technology Meeting, EUROMEDECINE 94, will take place in Montpellier, France, from 10–13 November 1994. The scientific programme will include: Unstable Mutations (10 Nov), Congenital Cardiopathies: Genetics, Morphogenesis, Diagnosis and Therapy (10 Nov), Genetics of Gametes and Human Embryos (11 Nov), Psychological, Sociological and Economic Aspects of Predictive Medicine (11 Nov), Microcytogenetics (12 Nov), Genetic Predisposition to Breast Cancer (12 Nov), Mitochondrial Genetics (13 Nov), Genetic Data Banks (13 Nov). Contact Josette Roudat in Paris (tel: 33. 1. 43 54 30 00, fax: 33. 1. 43 54 85 91) and Anne-France Rouquette in Montpellier (tel: 33. 67 13 61 19, fax: 33. 67 13 61 10).