

there is unlikely to be major confusion between the two groups.

The limb-girdle muscular dystrophies (LGMD) are a group of autosomally inherited progressive myopathic diseases. Eight different genetic types of LGMD have so far been identified, of which two are dominantly inherited and the other six recessively inherited.¹ Of the genes so far identified, three encode structural proteins of the dystrophin associated glycoprotein complex and one encodes the muscle specific calpain. Clinically, there are insufficient data so far to distinguish between the different forms of LGMD.

In the past, LGMD has been confused with other forms of muscle disease. Patients previously diagnosed as suffering from LGMD have in some cases been shown by molecular analysis to have a dystrophinopathy (X linked) or mitochondrial or metabolic disease.

Given the extreme heterogeneity of LGMD, it is important to ensure that resources applied to track down the primary genetic defect in any particular family or case are appropriately directed by careful exclusion of all possible alternative diagnoses. It has been postulated that the milder forms of spinal muscular atrophy (type III SMA) may be a source of diagnostic confusion in recessive or sporadic cases. Phenotypically, both diseases show proximal muscle weakness and wasting, creatine kinase levels may be raised in SMA, and EMG and muscle biopsy analysis may show conflicting or confusing results.

It is now possible to perform molecular tests for the genetic faults which are associated with chromosome 5 linked SMA. We examined a panel of 95 patients with a diagnosis of LGMD. These patients were from a variety of different sources both in the UK and abroad. Some referred themselves to our department because of our research interest in LGMD, others were referred from recognised neuromuscular units. All, according to the information available, had clinical characteristics and investigations which were consistent with a diagnosis of LGMD according to the latest diagnostic criteria.²

We analysed DNA samples for deletions of exons 7 and 8 of the survival motor neurone (SMN) gene (deleted in approximately 94% of milder SMA cases)³ and also for deletions of exons 5 and 6 of the neuronal apoptosis inhibitory protein (NAIP) gene (deleted in about 67% of SMA type 1 cases and 42% of type 2 and 3 cases).⁴ We found deletions in SMN and NAIP in only one family. Haplotype analysis confirmed that the affected sibs in this family did share the chromosome 5 region containing the SMN and NAIP genes. The three children from this family had childhood onset of a predominantly proximal muscle weakness and wasting diagnosed clinically and on investigation as a limb-girdle muscular dystrophy. Recent re-evaluation of serum creatine kinase showed that the level remained high (576 IU/l, normal up to 180 IU/l) even many years after the onset. All had relatively slow progression of disease and normal intelligence.

We conclude that spinal muscular atrophy associated with deletions of SMN and NAIP is not a common source of confusion in the diagnosis of LGMD. The investigation may, however, still be useful in those families in which there is genuine diagnostic confusion on the basis either of equivocal creatine kinase levels or conflicting results from EMG or muscle biopsy.

We are very grateful to the patients and clinicians who have helped collect the samples for this and other studies. Financial support has been provided by the Medical Research Council of Great Britain, the Muscular Dystrophy Group of Great Britain and Northern Ireland, and the British Medical Association.

R POGUE
T JACKSON
B SAYLI
A CURTIS
K M D BUSHBY

Department of Human Genetics, University of Newcastle upon Tyne, 19/20 Claremont Place, Newcastle upon Tyne NE2 4AA, UK

- 1 Bushby K, Beckmann JS. Report of the 30th and 31st ENMC International Workshops. *Neuromusc Disord* 1995;5:337-44.
- 2 Bushby K. Diagnostic criteria for the limb-girdle muscular dystrophies: report of the ENMC Consortium on limb-girdle muscular dystrophies. *Neuromusc Disord* 1995;5:71-4.
- 3 Lefebvre S, Burgler L, Reboullet S, et al. Identification and characterisation of a spinal muscular atrophy-determining gene. *Cell* 1995;80:155-65.
- 4 Roy N, Mahadeva MS, McLean M, et al. The gene for neuronal apoptosis inhibitory protein (NAIP), a novel protein with homology to baculoviral inhibitors of apoptosis, is partially deleted in individuals with type 1, 2 and 3 spinal muscular atrophy. *Cell* 1995;80:167-78.

BOOK REVIEWS

If you wish to order or require further information regarding the titles reviewed here, please write to or telephone the BMJ Bookshop, PO Box 295, London WC1H 9JR. Tel 0171 383 6244. Fax 0171 383 6662. Books are supplied post free in the UK and for BFPO addresses. Overseas customers should add 15% for postage and packing. Payment can be made by cheque in sterling drawn on a UK bank or by credit card (Mastercard, Visa, or American Express) stating card number, expiry date, and full name. (The price and availability are occasionally subject to revision by the Publishers.)

Cell Therapy. Editors G Morstyn, W Sheridan. (£70.00, US\$100.00.) Cambridge: Cambridge University Press. 1996. ISBN 0-521-47314-2.

It has been predicted that in the coming decade cell based therapies will begin to rival traditional pharmaceuticals in many areas of medicine but especially oncology. This timely book largely succeeds in its goal of providing a snapshot of this rapidly expanding field. The more than 70 contributors are authorities in the field and this amply compensates for the inevitable variation in how up to date the material is.

The book is organised into sections covering overlapping scientific, technical, and clinical aspects of haematopoietic cell therapy and immunotherapy introduced by succinct reviews of relevant aspects of the haematopoietic and immune systems by Moore and Slavin. The main body of the book is devoted to laboratory and clinical aspects of haematopoietic cell therapy starting with excellent reviews of progenitor assays, flow cytometry, and gene transfer technology. Mobilisation of peripheral blood progenitor cells, perhaps the major advance in haematology in the last decade, is well covered in a series of chapters by Shpall, To, and Sheridan and this is

followed by reviews of cell selection, purging, and expansion by some of the innovators and authorities in the field. The reason for the development of these technologies is, of course, that they facilitate dose intensification strategies in the treatment of malignant disease, and approaches to this involving growth factor and cellular support in a variety of diseases are covered next. Discussion of future applications of haematopoietic cell therapy is restricted to gene therapy and cellular therapy of HIV disease, areas in which success to date has been modest to say the least. Techniques for the generation of dendritic cells, perhaps one of the most promising new developments, are scarcely mentioned and this must count as a major omission. The final section of the book concentrates on experimental and clinical aspects of immunotherapy with coverage of neutrophil transfusion, tumour vaccines, and adoptive immunotherapy with autologous T and natural killer cells and allogeneic cells in the context of bone marrow transplantation.

Inevitably some relevant topics are not covered. As noted above, dendritic cells are only mentioned in passing and a chapter on T cell depletion, perhaps the commonest type of "graft engineering" currently performed, would have been helpful. Regulatory issues do vary from country to country but there are common safety concerns and discussion of these would also have been useful. Overall, however, these omissions do not detract from the value of the book which will be of interest to scientists, clinicians, and those in the biotechnology and pharmaceutical industries.

STEPHEN DEVEREUX

DNA and Protein Sequence Analysis. Editors M J Bishop, C J Rawlings. (£29.95.) Oxford: Oxford University Press. 1997. ISBN 0-19-963463-7.

This book is intended for biologists wishing to understand more about molecular biology databases and methods of sequence analysis. As the editors state in their preface, it is 10 years since the publication of the similarly titled "Nucleic Acid and Protein Sequence Analysis" in this series and a new volume is certainly welcome. There are very few books covering this area and information is scattered in original papers and software manuals. On the technical side, one of the most noticeable changes in working methods has been the use of the World Wide Web to access databases and software. I felt that while the preface emphasised this, some of the earlier chapters that concentrated heavily on software were rather dated, partly as a result of the time taken to publish such a book.

It would have been helpful to have a longer introduction to the book to tie together the material. For example, there was no explanation of why one chapter was devoted to software for the Macintosh (10 years ago a similar chapter referred to the PC). There is a wide variation in style between authors and in the prior mathematical and computing knowledge assumed. Some biologists will undoubtedly feel that much of this book is about theory and not practice, though this is very much a feature of the subject.

Many of the later chapters give a better balance between the theoretical background and the software to perform the analyses. This was especially true of the chapter on Phylogenetic Estimation by Dr N Goldman,

which also contains strong caveats and useful pointers to future research. Where possible, it would be helpful if a similar style and balance were to be used throughout the next sister volume, which we may hope to see in less than a decade, given the rapid growth in this field.

JENNY BARNA

Gene Therapy Protocols. Methods In Molecular Medicine. Editor Paul D Robbins. (Pb \$74.50.) USA: Humana Press. 1996. ISBN 0-896-03307-4.

During recent years, the field of gene therapy has evolved into an area of intense research. Investigations in the field cover a wide range of disciplines into delivery vehicles (involving chemical, biochemical, and virological studies), administration of genetic material, as well as elucidating the genetic causes of disease. Publications such as "Gene Therapy Protocols" are invaluable, bringing together information from an extremely wide source of reference in one volume. In addition it presents up to date protocols used in gene therapeutic approaches and includes useful notes and background information on the subject.

The title of the book implies that it is simply a collection of methods used for gene transfer, with individual chapter headings being somewhat deceptive. One could be forgiven for thinking how, for example, "Methods for targeted gene transfer to liver using DNA-protein complexes" (chapter 10) would be applicable to other areas. Indeed, though this chapter concentrates its information on the subject in the title, the techniques outlined are available to modification for other applications.

The content matter of the book is impressive. There are representative chapters for almost all aspects of current research in gene therapy, including generation of vectors, vector delivery (*ex vivo* and *in vivo*), and cancer gene therapy. Additionally, there are details regarding histological examination of tissues, cell biology, and cancer genetics.

The notes sections at the end of each chapter can be particularly useful. Contained in these sections are details regarding the parameters which it is necessary to consider for optimisation of the systems. For example, a note at the end of chapter 8 ("Methods for liposome-mediated gene transfer to the arterial wall") outlines the necessity of altering the DNA:lipid ratio for each cell line and each lipid formulation. While this may be obvious to some readers, it may be of great relevance to others.

It is difficult to suggest who the book would be most suitable for. To the casual reader or student, it may appear difficult reading, but sufficient background information is contained to maintain their interest. Similarly, to the researcher in the field, some areas may appear tedious, but again the ample detail should keep their attention.

In summary this book is a valuable addition to a library or laboratory involved in gene therapy research and should be read by a significant cross section of students and academics owing to both the wide breadth and detailed nature of the information contained.

JEFF DREW
J GEORGE DICKSON

NOTICES

China's eugenics law. A position statement of the Canadian College of Medical Geneticists

Preamble. The Canadian College of Medical Geneticists appreciates the aim of the Chinese Government to reduce the frequency of serious, genetically determined disorders in the population, but does not believe that to impose restrictions on reproduction of at risk couples is a good way to achieve this end, since (a) for most serious genetic disorders, preventing reproduction of those affected by, or carrying, the alleles for such disorders will not achieve significant reductions in frequency of those disorders, since they are already rare, for most of them the probability of occurrence in the offspring of affected individuals is low, and selection against recessively inherited disorders is very ineffective; (b) for the minority of serious genetic disorders that are not rare, and for which the carriers can be detected, programmes of voluntary genetic screening, counselling, and prenatal diagnosis can achieve major reductions in frequency.

Therefore, the CCMG supports any measures that will improve communications with Chinese geneticists, physicians, and legislators, including the training of students, collaborative research programmes, and attendance at scientific meetings, with the aim of helping to persuade the Chinese government to replace its programme of negative eugenics with a programme of public education, genetic screening, and voluntary prenatal diagnosis.

This statement was prepared by the Ethics and Public Policy Committee of the Canadian College of Medical Geneticists and endorsed by its Board of Directors, June 1997.

GENATLAS on line

The database GENATLAS is now open on the web, through the server INFOBIOGEN, at the following address: <http://www.infobiogen.fr>

The GENATLAS database compiles, from published reports, the information relevant to the mapping of genes, diseases, and markers. Further information is provided on the category to which the objects belong, that is, growth factor, their structure, polymorphism, function, their spatiotemporal or differential (imprinting) expression. These features contribute to the specificity of GENATLAS as well as the strong emphasis put on the clinical disorders. They are classified by organ, tissue, or affected system (for example, eye disease) and according to their category. Besides the mendelian diseases, chromosomal rearrangements and breakpoints associated with developmental abnormalities or malignancies are compiled in GENATLAS. The information relative to genes, diseases, and objects is accompanied by pertinent citations, as well as by linkage data, maps, and information on comparative mapping edited by John H

Edwards. GENATLAS is interactively linked to the Location Database of Newton E Morton. GENATLAS is also linked to OMIM, Medline, and the nucleotide sequence databases.

Interested people are kindly requested to refer to the presentation on GENATLAS, on the web, to become acquainted with GENATLAS (see About) and to make their advice, comments, and criticism known to Professor Jean Frézal, editor (Service de Génétique Médicale, Hôpital des Enfants Malades, 149 rue de Sèvres, 75743 Paris cedex 15, France. Tel: 01 44 49 51 54, Telecopie: 01 40 56 34 97. E mail: frezalj@necker.fr

GENATLAS is also incorporated into a CD-ROM with PC and Macintosh versions.

GID, Genome Interactive Databases

GID gathers the GENATLAS and comparative directories into the CEPH (index, lod, YACs) databases, to the GENETHON microsatellites database and to the Location Data Base (LDB).

Publisher: John Libbey Eurotext, 127 avenue de la République, 92120 Montrouge, France. Tel: 00 (0)1 46 73 06 60. Fax: 00 (0)1 40 84 09 99.

The newest issue of GID will be available in September.

IMGT database

IMGT, the international ImMunoGeneTics database, announces a standardised description of allele polymorphisms and mutations for all immunoglobulin and T cell receptor V-REGIONS of all species, based on the IMGT unique numbering (IMGT NEWS, March 1997). Allele alignments and tables for the human IGH, IGK, and IGL V-REGIONS are freely available at IMGT <http://imgt.cnusc.fr:8104>.

IMGT initiator and coordinator: Professor Marie-Paule Lefranc, Laboratoire d'ImmunoGénétique Moléculaire, LIGM, UMR 5535 (CNRS - Université Montpellier II), 1919 route de Mende, 34293 Montpellier Cedex 5, France. Tel: +33 (0)4 67 61 36 34. Fax: +33 (0)4 67 04 02 31. E-mail: lefranc@ligm.crbm.cnrs.mop.fr

IMGT reference: Giudicelli *et al. Nucleic Acids Res* 1997;25:206-11.

11th Course of the International School of Biomedical Sciences

The Institut Louis-Jeantet d'histoire de la médecine in collaboration with the Wellcome Institute for the History of Medicine, London, and the support of the Fondation Marcel Mérieux and the Fondation Louis-Jeantet de médecine, is organising the 11th Course of the International School of Biomedical Sciences on the subject "The burdens of the past: heredity in medicine from constitution to molecular genetics". The course will be held at the Pensières Conference Centre (Fondation Mérieux), Annecy, France on 1-10 July 1998. Applications should be sent by 30 April 1998 to Institut Louis-Jeantet d'histoire de la médecine, CMU, Case postale, 1211 Genève 4, Switzerland. Tel: +41.22.702.57.90. Fax: +41.22.702.57.92. E-mail: Bernardino.Fantini@medecine.unige.ch