Familial predisposition to both male and female germ cell tumours

A minority of testicular teratomas are recognised to be familial.1 Some occur as part of the spectrum of cancers in the Li-Fraumeni syndrome; however, the genetic basis of the majority of familial cases is unknown. This has hampered the formation of a large consortium to identify genes causing testicular teratomas. As one of the participating centres we have been ascertaining familial cases from a registry of testicular teratoma patients in the Royal Marsden Hospital, Sutton, Surrey. Among these cases we have identified three families which suggest that a common genetic basis exists between some male and female germ cell tumours.

The first family was identified through an index case who presented with a seminoma at the age of 51, his brother had had a testicular teratoma at the age of 28, and their cousin an endodermal sinus tumour of the ovary diagnosed at 32 years. In the second family the index case presented with an undifferentiated malignant teratoma at 28 years of age and his sister was diagnosed with bilateral malignant teratomas at the age of 39. In the third family the index case presented with a retroperitoneal teratoma at 26 years and his sister was diagnosed with an ovarian teratoma at 45 years. None of these families had any features indicative of the Li-Fraumeni syndrome or any other cancer family syndrome, suggesting the identification of a previously unrecognised association. This is supported by two reports of single families with ovarian and testicular germ cell tumours3 and a family with multiple cases of dysgerminoma.4 The three families we report were identified from a database of 2000 teratoma patients, suggesting that in 0.2% of pedigrees a female member will develop a germ cell tumour. This may be an underestimate since pedigree information on all 2000 index cases has not been verified and many mature teratoma cytoses are asymptomatic and go undiagnosed.

Whether an association between male and female germ cell tumours is the result of the inheritance of a single genetic defect common to both ovary and testis or a consequence of the action of modifying genes will only be established when the gene or genes causing testicular teratomas are identified.

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BOOK REVIEWS

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The many advances and widespread use of prokaryotic and eukaryotic protein expression systems is reflected in the increase in the size of this text, from four chapters in the first edition 10 years ago, to a complete volume in 1995 with an additional volume dedicated to mammalian systems. This volume provides a clearly written text covering the major aspects of protein expression, from the isolation of a cDNA through to the purification of the expressed protein product and the generation of antibodies to that product. Systems covered include fusion and non-fusion protein expression in E coli, protein production, two hybrid interaction screening in yeast, and baculovirus expression of protein in yeast and insect cells. The generation of polyclonal and monoclonal antibodies to expressed proteins is also covered in some detail. The text provides sufficient introduction and background for a complete understanding of the methodology under discussion, with detailed protocols presented in clearly marked boxes within the text, often containing handy notes and tips from the authors.

This volume would be entirely sufficient for someone outside the field to isolate a CDNA to a protein of interest, clone into an appropriate expression vector, achieve soluble protein expression, and raise antibodies as well as investigate possible other protein-protein interactions. It is more than a list of protocols, it provides a concise account of the "whys and wherefores" of the methods being used. As the individual chapters "stand alone", there is some duplication where the reader is given methods for SDS-PAGE or western blotting in more than one chapter, but this is a minor irritation. The only aspect of protein expression that is not covered, neither in this volume nor apparently in volume 4, is the production of protein in rabbit reticulocyte lysates, a rapid method for the generation of small quantities of correctly folded protein (often labelled) for the determination of protein-protein interactions or other functional assay. It is inevitable, however, as the editors hope, that this book will become "dog-eared" from constant use in the laboratory, both as a source of reference and as a practical guide.

STEVE WINDER

The 4th International Symposium on Epitope and Morphogenesis of Congenital Heart Disease was held in Tokyo in November 1993. The editors' stated aim in this volume is to allow the participants of the symposium to share their knowledge with a broader audience of scientists and clinicians. The book includes the symposium's abstracts as well as commissioned overview chapters and has been divided into six main sections and 72 papers or overview chapters.

The first section reviews the cellular biology and the molecular analysis of cardiac developmental phenotypes including gene expression during embryonic development. The second section extends the application of molecular biology to medical genetics especially the cardiomyopathies. The third and largest section overall is divided into four overview and 26 papers related to wider ranging aspects of congenital heart disease including the aortic arches, the right heart development as well as tetralogy of Fallot, and other specific congenital abnormalities. Aspects of the functional development of the heart are contained in the final section.

The penultimate section entitled "Human and Animal Models of Cardiac Defects" focuses particularly of interest to clinicians covering congenital abnormalities and laterisation defects as well as an interesting review of...
abnormalities of the branchial arch in 45, XO fetuses. There is a final sixth section on the epidemiology of congenital malformation.

Overall the illustrations are relevant and well-supported. The chapters are referenced and indexed. Such a collection of papers as well as overview chapters is an extremely extensive and useful source for those with an interest in the developmental mechanisms of heart disease but does tend to lead to repetition, unlike a textbook. As an illustration there are several overlapping papers dealing with deletion of chromosome 22q11 and similarly heterozygous and the inv mutation in the mouse. The quality of the papers is variable but overall the editors’ initial aim is achieved with the book providing an interesting review of current understanding of some of the mechanisms in developmental heart disease. It would be a welcome addition to the library of any department with an interest in cardiac genetics.

SALLY DAVIES


Given the handling, storage, and disposal problems associated with radioisotopes such as P-32 and I-125, there has been a drive to circumvent their use as detection agents in standard molecular biological techniques. This laboratory manual is a compendium of methods for the use of bioluminescence, chemiluminescence, electrochemiluminescence, fluorescence, and colorimetry as alternatives in various types of blotting, quantitative PCR, and DNA sequencing. The book is subdivided into three sections; the first of these (“Introduction”) consists of two chapters which provide an overview of non-radioisotopic labels available and the range of techniques to which they may be applied. Chapter 2 is particularly good as a general guide to the synthesis of both DNA and RNA probes and incorporates discussion of enzymatic and chemical means of labelling. The “Detection Module” comprises 16 chapters in which individual methods are considered in more detail by authors involved in their development. Each chapter is relatively self-contained, providing detailed experimental protocols for the use of a given detection system, including step by step methods for the synthesis of suitable probes and the consideration of possible problems arising in the implementation of these techniques. Nine chapters in this section discuss direct or indirect conjugation of enzymes such as alkaline phosphatase and horseradish peroxidase to nucleic acid probes. This serves to emphasize the versatility in generating detectable signals from a wide variety of substrates according to the application and level of sensitivity required. Also considered in this section (five chapters) are the use of lanthanides such as europium and ruthenium chelates, for time resolved fluorescence and electrochemiluminescence. One chapter covers the generation of chemiluminescent signals through use of acridinium esters, while the remaining chapter deals in some detail with the use of fluorescence energy transfer based assays. The final part (“DNA Sequencing”) is composed of two chapters, covering chemiluminescent and fluorescent detection methods. In the latter, a brief section on automated sequencing is also included, although manual detection methods are discussed predominately. In general, the physical and chemical principles behind each detection system are well explained and illustrated with clear diagrams throughout the book. In conclusion, although the implementation of some of the methods described may involve considerable financial outlay for detection hardware, this manual would be a useful source of information in any laboratory where molecular biological assays are used on a regular basis.

LUCINDA REYNOLDS


The authors have considerable experience in the rapidly developing field of inherited connective tissue disorders. They emphasise the need for accurate diagnosis which still relies heavily on careful clinical and radiographic assessments. This atlas provides an illustrated guide to many of these disorders and correlates the clinical, radiological, and pathological features with the molecular defects, where known.

The first chapter provides an introduction to the classification of connective tissue disorders, the composition of connective tissues, and the main clinical features.

Chapters 2 to 7 provide detailed information on Ehlers-Danlos syndrome, Marfan syndrome, pseudoxanthoma elasticum, cutis laxa, osteogenesis imperfecta, and other connective disorders. Chapter 8 includes the osteochondrodysplasias. The authors have excluded the mucolipidoses and the mucopolysaccharidoses.

All chapters are superbly illustrated. The clinical photographs are in colour and clearly show the points referred to in the figure legends. The histological and radiographic illustrations are also well presented. Some chapters contain protein electrophoretic gels and DNA sequencing gels to illustrate the underlying molecular defects. Some additional labelling for the electrophoretic gels would be useful for readers who are not expert in connective tissue biochemistry.

This atlas is a valuable reference for departments and clinics that care for families with inherited connective tissue disorders, particularly disorders of the skin as well as Marfan syndrome and osteogenesis imperfecta. The chapter on osteochondrodysplasias occupies only 13 of the 146 pages of this atlas. It is well illustrated, but it could be usefully expanded.

W G COLE

NOTICES

The Fifth International Congress on Trace Elements in Medicine and Biology: First United States FDA Medical Device Update: Design Controls, GMP Requirements and Marketing Clearance

This meeting will be held on 2-23 May 1996 at Charles-de-Gaulle Hilton, Paris, France. An international meeting on FDA GMP and marketing regulations including the proposed new GMP requirements and how to comply with them. All three days will be presented by FDA’s CDRH with a presentation by the European Commission. Sponsored by the French Government. Contact: Zena Barrick, Medical Device Technology, Advanstar House, Park West, Stockton. Tel: +44(0)224 378 888, Fax: +44(0)224 370 011.

Quality of Life: An International Conference for Families and Professionals on Developmental and Related Disabilities

This conference will be held on 6–8 June 1996 in Toronto, Ontario, Canada. For further information contact Quality of Life Conference – Surrey Place Centre, c/o Continuing Education, 150 College Street, Room 121, Toronto, Ontario, Canada M5S 1A8. Tel: (416)978-2719, Fax: (416) 971-2200, e-mail a.lind@utoronto.ca.

Isozymes, Genes, and Gene Families

The 9th International Congress on Isozymes, Genes, and Gene Families will be held on 14–19 April 1997 in San Antonio, Texas, USA. For further information, contact Ms Daphne Wright, Congress Liaison, Southwest Foundation for Biomedical Research, PO Box 28147, San Antonio, TX 78228-0147, USA, Fax: 210-670-3337, e-mail: isozyme@darwin.sfb.org.