children. With advances in medical therapeutics there are an increasing number of patients with genetic disorders who previously may not have reached reproductive age. This is particularly so in the area of genetics dealing with inborn errors of metabolism. The book largely deals with one of the commonest metabolic disorders, phenylketonuria. It focuses on the advances in management of maternal PKU and the implications of lack of dietary control to the unborn fetus. The chapter on carrier females of ornithine transcarbamylase deficiency highlights the importance of thinking of inborn errors of metabolism in women who present with post partum coma, which has been reported to be confused with puerperal psychosis.

The book is well written and gives an update on maternal aspects of a few inborn errors of metabolism. Its title, however, initially suggests a much broader scope and to this end is disappointing. A wider reader population may have been captured if other genetic disorders, such as myotonic dystrophy, collagen disorders such as Marfan syndrome, Ehlers-Danlos syndrome, and osteogenesis imperfecta, neurofibromatosis, inherited thrombophilias, and haemoglobinopathies, for example, had been discussed. Many pose management issues not only in terms of prenatal testing, but also for the obstetric management of the mother. Discussion of the haemoglobinopathies could, of course, highlight recent research of the role of stem cell transplantation as in utero therapy in a variety of disorders.

This book uses PKU as an example of a genetic disorder that raises issues in management of the mother and the fetus. To this end, it provides a model for assessment of other metabolic disorders where a pregnant woman may be at risk.

ROBERT OGLE

The Book of Man: The Human Genome Project and the Quest to Discover Our Genetic Heritage. Walter Bodmer, Robin McKie. Oxford: Oxford University Press. 1997.

"The Book of Man" was first published in 1994 to report the breaking story of the Human Genome Project in the popular science idiom. This review is prompted by the issue of an OUP paperback edition, which I suspect contains few if any changes from the original version. The authors recount the history and describe the biology underlying "one of mankind's greatest odysseys" in a digestible form for a wide audience. The scope is broad, with chapters on genetic engineering and the birth of pharmacogenomics, gene mapping and positional cloning, cancer and behavioural genetics, forensic and evolutionary applications, and genetic diagnosis and therapy. The narrative style is inviting and the reader rapidly becomes attuned to the distinctive voice of Walter Bodmer who seldom flinches from hyperbole. Anecdotes, scattered throughout the text, add human interest to the science. The vocabulary includes many technical terms that might well perplex some; it would have been useful to include a glossary.

Bodmer and McKie's mission is to "inculcate" DNA literacy into society so that we will have a better understanding of the "essence of being a human" and understand "our role in evolution and survival as a species". The

pervasiveness of genes on human experience is claimed in the very first chapter, where Sir Walter introduces one of his pet projects, the inheritance of perfect pitch, to illustrate his reductionist vision that "one by one" genes that contribute to "any complex human quality" will be identified. The overall message is crystal clear, advances in human genetics are enriching many aspects of our lives and alleviating suffering at an acceptable cost whether in terms of personal freedom, religious conviction, moral standpoint, or animal experimentation. It is hoped that a better educated public will be more receptive to genetic innovation, although emotional responses seem to be trusted more than analytical solutions nowadays.

I have not seen earlier hardback editions to assess the relative production qualities but I was somewhat disappointed by the pictorial content. For example, the photographs of Ferniehurst Castle, Watson and Crick, and Franklin and Gilbert are poor quality reproductions that fail to enliven the text. A monochrome version of a map that I guess was originally drawn in colour to show the pattern of migration during human evolution is difficult to read. I also felt that some of the drawings would be difficult to comprehend or put into context by those with limited biological training. For example, it is hard to appreciate the scale of a line drawing of a polyp and the schematic of DNA replication contributes more to iconography than comprehension. I also thought that the accuracy of diagrams illustrating chorionic villus sampling (CVS) and amniocentesis could be improved.

If an updated version of this book is published then I hope that the opportunity is taken to revise the graphics. The authors might also reconsider their lack of concern for "the intrigues and politics of this great scheme", which make fascinating reading. In the meantime, this book will continue to make its unapologetic pitch to western society to invest in the widest sense in the human genomics project.

MARTIN FARRALL

Oligonucleotides as Therapeutic Agents. Ciba Foundation Symposium 209 held on 7-9 February 1997. (£55.00.) UK: John Wiley. 1997. ISBN 0-471-97279-7.

The use of antisense and catalytic oligonucleotides in gene therapy has promised much, but, like the higher profile viral vectors, has failed to deliver consistently in terms of therapeutic benefits. Despite this, the logic in using oligonucleotides remains intellectually very appealing. Therefore, a report on the current state of play is timely. Although lacking the glossy additions increasingly found in books, the monograph represents the proceedings of a Ciba Foundation Symposium on "Oligonucleotides as Therapeutic Agents" held in early 1997, and so the editors and publishers have performed well to achieve a relatively short publication time. Contributors come from varied backgrounds including academic and biotechnology. A relative paucity of input from clinically based groups confirms the impression that oligonucleotides are a long way off as potential challengers to current approaches for gene therapy. Nevertheless, the book will appeal to a broad group of readers from researchers to clinicians who have a common interest in gene therapy. It will provide a useful and up to date reference source for libraries. Three broad

themes are covered: chemistry and production; pharmacology and in vitro studies; and therapy.

Chapters 2, 3, 16, and 18 (my numbering) deal with industrial approaches to production of oligonucleotides including future options to enable large scale but cheap output (for example, it is estimated that 2.5-5 kg/year of oligonucleotides would be required for prevention of restenosis following angioplasty). I found chapter 18 particularly interesting with its preliminary description of how a bacterially derived reverse transcriptase might be used to produce oligonucleotides in vivo. Just as the present vectors for gene transfer will require considerable development before they can achieve useful therapeutic benefits, our knowledge of the oligonucleotide's chemistry is clearly shown to be in the early stages and so the field remains open to inventive minds.

Chapters 5 and 6 provide useful insight into the pharmacokinetics of various types of oligonucleotides using both animal and tissue culture conditions. The importance of better methods of cell delivery and improved intracellular half life remain sticking points with oligonucleotides. Attempts at quantitating internalisation and compartmentalisation of oligonucleotides are made in chapter 7. A brief review in chapter 4 shows how different regions of mRNA respond to oligonucleotides, hence the importance of selecting the appropriate sequence. A method by which this could be achieved is discussed. Chapter 8 focuses more on the use of triple helix formation and illustrates the value of these oligonucleotides by reference to in vitro studies using HIV and the IL2 receptor gene. Chapter 11 describes physical means (microinjection and lipids) by which oligonucleotides can be taken up by cells.

My own particular interest, that of clinical applications and potential successes in the use of oligonucleotides as gene therapy agents, was generally satisfied by chapters 12-15. Chapter 12 was a little disappointing in that reference was made to therapeutic achievements being obtained for a phase II study in Crohn's disease and a phase III study in CMV retinitis. However, details were very scanty. The same contributors illustrated ways (chapter 9) in which commercially produced oligonucleotides against c-ras could be used as a form of anticancer therapy. Chapter 13 provided a lot more information about efforts to interfere with c-myc expression, a gene considered to play a role in leukaemogenesis. Both in vitro and in vivo studies (the latter using a leukaemia/SCID mouse model) are described in which oligonucleotides downregulated c-myc. A human trial is briefly mentioned to illustrate how oligonucleotides could function to purge chronic phase bone marrow before transplantation during the blast phase of chronic granulocytic leukaemia. The problems of the oligonucleotide's chemical composition, the reliable delivery in vivo, the importance of targeting, the long term effectiveness, and the host's immune responses are noted in this chapter (as well as a useful review in chapter 1) as areas which still require considerable developmental work. Chapter 15 summarised in vitro and animal model studies using ribozymes as oligonucleotides to inhibit expression of the MDR1 gene and a number of other clinical disorders including HIV infection. Comments made, as well as feedback from the floor, confirmed that ribozymes, although more attractive because of their

catalytic activities, are even less well studied for their *in vivo* effects.

RON TRENT

The Yeast Two-Hybrid System. Editors Paul L. Bartel, Stanley Fields. New York: Oxford University Press. 1997. ISBN 0-19-510938-4.

It is now difficult to open a life science journal without reading at least one paper with the sentence "a yeast two hybrid screen was performed..." so the arrival of this attractively produced book caused a stir in my laboratory. It is written by the people who developed the system. Late one afternoon in 1987, Stanley Fields (then a new assistant professor at SUNY in a small laboratory working on an obscure aspect of yeast pheromone responses) suddenly realised that he could use two different hybrid proteins, one containing a DNA binding domain and the other a transcription activation domain, to detect protein-protein interactions. He immediately recognised that it might be feasible to use the system to search cDNA libraries to find novel protein partners. It is ironic that a seed grant proposal written later that same year was rated by the review panel as "having no possibilities for commercial development" and the research was eventually supported by Procter and Gamble. Eleven years later Fields and his colleagues must feel entitled to a quiet glow of vindication as they survey the honour roll of proteins pulled out of yeast two hybrid screens. For example, in working out cell cycle checkpoint control during the early 1990s, the CDK inhibitors p16, p18, p19, p21, and p27 were all discovered by different groups using the system.

Many people will buy the book for the three early chapters which describe the nuts and bolts of manipulating yeast and performing a basic library screen. Each of these chapters is devoted to one of three different systems that have been developed by different groups over the years. The protocols are clear and sufficiently detailed to allow someone who has never worked with yeast to perform a two hybrid screen (chapter 3 is an improved and more detailed version of a much photocopied protocol which our laboratory has used successfully over the past three years). We have found that the scientists who developed the system are generous with their time and reagents and this impression is reinforced by the list of laboratory web pages, e-mail addresses, telephone and fax numbers at the end of chapter 4. These first four chapters justify the price of the book. I also enjoyed the clear description of the ingenious reverse two hybrid system for mapping critical residues in protein-protein interactions and will use the protocols presented here, which seem straightforward. A chapter on constructing activation domain-fusion libraries did not provide much more information than can be obtained from Maniatis. Other chapters are more descriptive or speculative; there are reviews of ligand-receptor interactions, cell cycle and signal transduction pathways which, although well written, cannot provide more than an overview in the space assigned to them, and I was disappointed that the one hybrid system which holds great promise for detecting DNA binding proteins was only given a brief space. The possibility of using the yeast two hybrid system to generate massive whole genome protein interaction connectivity networks in

the "post-genomic future of the 21st century" is discussed in a very readable chapter; it sounds like science fiction, but given the achievements of the yeast community in the last decade, I wouldn't be surprised if they pull it off.

LUKE HUGHES-DAVIES

Genetics. A Molecular Approach. 3rd edition. T. A. Brown. (£27.50.) London: Chapman and Hall. 1998. ISBN 412 798700.

The field of molecular genetics is vast and complex with its own extensive vocabulary and it is hard for a novice to approach it without feeling daunted. However, an understanding of genetics is now essential for most undergraduate and postgraduate science and medical students. This well written book will be welcomed by both newcomers and experienced geneticists as well as those who teach the subject to undergraduates.

Starting with DNA rather than Mendel, the author tells the story of genetics in three parts. In part 1, he explains the structure of DNA and the chemical nature of the gene with chapters describing control of gene expression and DNA replication, mutation, repair, and recombination. In part 2, genes are put into the context of genomes, both prokaryotic and eukaryotic, with an excellent chapter describing the structure of the human genome including gene families and pseudogenes, extragenic DNA, and polymorphisms. Part 3 describes patterns of inheritance with sections on Mendel's experiments and their subsequent molecular explanations, genetic linkage, the human genome mapping project, and an overview of the techniques currently used in the molecular biology laboratory. An historical context is maintained throughout the book with descriptions of landmark experiments such as those used by Hershey and Chase in the 1950s to show that genetic material is DNA and not protein.

The text is clear, succinct, and liberally illustrated and no new term is introduced without being defined and listed in the extensive glossary. The author is clearly an experienced teacher of his subject and has written a book which is both readable and informative. I would have no hesitation in recommending this book to anyone needing a thorough grounding in molecular genetics.

JULIA RANKIN

The Calculation of Genetic Risks: Worked Examples in DNA Diagnostics. 2nd edition. Peter J. Bridge. (£34.50.) Baltimore: The Johns Hopkins University Press. 1998. ISBN 0-8018-5744-9.

Apart from a few exceptional people, I think that geneticists, whether clinical or in the molecular diagnostic laboratory, are not particularly mathematically inclined. Indeed, I am fairly certain that there are many, including me, who develop a curious form of mental fugue when faced with the more complex risk calculations that we sometimes come across in clinical genetic practice. Peter Bridge's book is written for us. The main aim of the book is to provide the reader with the skills required to formulate sensible risk calculations, and it takes a very practical approach, building from problems which use only pedigree information to increasingly

complex problems incorporating biochemical and molecular genetic information. The problems are not abstract; service geneticists could expect to meet very similar ones on a regular basis. The particular beauty of this book lies in its comprehensibility. Rather than inflicting difficult equations on us, the author instead uses clarity of ideas and expression, and emphasises general principles. My one criticism is the lack of "self-test" problem sections at the end of each chapter, which would allow readers to really test their new understanding. However, I would unhesitatingly recommend this book to clinical geneticists, molecular geneticists in diagnostic laboratories, and to anyone who wants to have a good grounding in the principles of risk calculation for genetic disease.

EVAN REID

NOTICES

British Human Genetics Conference

The British Human Genetics Conference will be held on 28-30 September 1998 at the University of York, England. There will be special sessions on: Practical approaches to methylation and imprinting; FISH: present and future; Predictive testing protocols - who benefits; The genetics of human behaviour; Human evolution; Joint symposium on multiple endocrine neoplasia with the Cancer Family Study Group, as well as plenary sessions. The Carter Lecture will be given by Professor Ken Kidd on "Evolution of modern humans". Further information from Professor Peter Farndon, British Society for Human Genetics, Clinical Genetics Unit, Birmingham Women's Hospital, Edgbaston, Birmingham B15 2TG, UK. Tel/fax: 0121 627 2634, e-mail: bshg@bham.ac.uk <http://www.bham.ac.uk/bshg>

The National Registry for Ichthyosis and Related Disorders

The purpose of this NIH supported registry is to improve methods of diagnosis, promote the search for basic defects, and develop more effective methods of treatment/prevention of the inherited scaling skin disorders. Affected people are asked to enrol through their local dermatologists. All contact information is kept confidential. Persons with ichthyoses (except ichthyosis vulgaris), erythrokeratodermas, Darier disease, Hailey-Hailey disease, palmar-plantar keratodermas, pachyonychia congenita, extensive epidermal naevi, and related disorders are eligible for enrolment. The Registry offers a means of "empowerment" for affected people and family members. It enables skin biologists, pharmacologists, and other investigators to share information about ongoing and future research with this well characterised group having specific diagnoses. For information please contact us at: The National Registry for Ichthyosis and Related Disorders, Box 356524, Seattle, WA 98195-6524, USA. Tel: 1-800-595-1265 or 1-206-616-3179, e-mail: ichreg@u.washington.edu or visit our web site at <http://weber.u.washington.edu/~geoff/ichthyosis.registry/> Philip Fleckman, MD, Principle Investigator Geoffrey Hamill, RN, Registry Coordinator