BOOK REVIEWS

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Tetrahydrobiopterin - Basic Biochemistry and Role in Human Disease. Seymour Kaufman. (Pp 420; £37 hardback.) Baltimore: The Johns Hopkins University Press. 1997. ISBN 0-8018-5344-3.

This is a well written and authoritative book. The author, Seymour Kaufman, and his research collaborators at the USA National Institutes of Health have contributed much to the subject; 17% of the 1300 or so references cited bear his name. I would specifically recommend it to readers of this Journal who have a particular interest in inherited metabolic disease. Its content serves to emphasise how our understanding of the biochemical, and clinical, phenotypic expression of mutant genes is highly dependent on our knowing, in precise mechanistic detail, how the gene product functions normally.

During the 1950s there began a major biochemical research effort aimed at discovering how molecular oxygen was used during enzymic hydroxylation of the ring structure of aromatic amino acids. Much of the stimulus for this activity derived from the knowledge that this reaction constituted the first step in synthesis of the "biogenic amine" neurotransmitter substances, and also that a defect in the hydroxylation of phenylalanine occurred in the recessively inherited neurological disease, phenylketonuria. This book describes in considerable detail the ensuing 40 years of scientific endeavour which has led to our contemporary knowledge of the structural and functional aspects of aromatic amino acid hydroxylation, including the unique cofactor requirement for these reactions in the form of reduced biopterin. This work, in turn, provides the scientific basis for our understanding of the inherited hyperphenylalaninaemias and, in particular, those rare variant forms owing to defects in the biosynthesis and recycling of tetrahydrobiopterin.

Approximately one quarter of the content is devoted to pathological aspects of the biochemistry described, although one might be tempted to criticise the title of the book as misleading for there is little here specifically related to biopterins. Nevertheless, the author provides a particularly comprehensive review of the many facets of the neurochemical pathology of the hyperphenylalaninaemias. This serves to remind the reader how much more work needs to be done in this area, not least because the clinical management of these conditions is, as yet, far from ideal.

Dr Kaufman then leads the reader on into exciting pastures new. Novel mechanisms in cellular metabolism are often later found to have a much wider functional role than the specific type of reaction where they first come to light. In this respect, the discovery of biopterin cofactors is no exception and of particular importance is the relatively recent recognition of their role in nitric oxide synthase activity. Among the topics of contemporary interest in biochemical physiology and pathology, few could be considered as important as that of nitric oxide and the extraordinary properties it possesses as a modulator of cellular activity in processes as diverse as vascular tonicity, central and peripheral neurotransmission, and cell mediated immunity. Undoubtedly the mechanisms which regulate the biosynthesis of such a highly reactive molecule will be of paramount importance in the control of its biological activity. This is an area of basic research very much in its infancy, and one in which the role of biopterins is yet to be fully explored.

It is perhaps in this respect that Dr Kaufman's treatise is most timely and welcome. On a firm foundation of current biochemical knowledge in a very specific area, he focuses the reader's mind on the work which remains to be done. Those who engage in this will be drawn from many different specialist fields in bioscientific research, including those which encompass the field of human genetics.

It is unfortunate, in these days of often inadequate budgets, that the price of this book will be a disincentive for its inclusion on the shelves of most departmental libraries. However, I would commend this book for consideration to those who advise on the acquisition of new material for their Institutional Libraries; in these it would be available for the wider readership it deserves.

A F HEELEY

Genome Structure and Function: From Chromosome Characterization to Gene Technology. Nato ASI Series (High Technology) volume 31. Editor Claudio Nicolini. (£99, US$170.) Dordrecht, The Netherlands: Kluwer Academic Publishers. 1997. ISBN 0792345657.

Rapidly moving fields in science spawn review style books that often struggle to be relevant much beyond their publication date. This view of the world of chromosomes and chromatin reported in the proceedings of the NATO Advanced Study Institute on Genome Structure and Function (held in June 1996), however, can still hold its own. The book achieves this by combining a series of in depth reviews interspersed with specialist chapters containing applications of chromosome and genome research, the topics covered ranging from oncology to biophysics.

The book opens with a chapter from the Editor, Claudio Nicolini, reviewing the biophysical methods used in unravelling the layers of successive folding the genome undergoes in order to be packaged into a functional chromosome. Subsequent excellent chapters then concentrate on padding out the detail of what these techniques have found with chapters discussing loop/domain models of chromosome structure (Razin), chromatin models (Belmont), and models of how the nucleosome functions in chromatin (Bradbury). From here we progress to chapters which concentrate on gene function and regulation within chromatin (Wolffe), steroid hormone regulation (Beato), and histone acetylation (Turner). This is the area of the book which suffers most from the passage of time and those wishing to be absolutely up to date would do well to follow up this very rapidly expanding area of research in more current journal based reviews. The applications of current gene technology and a hint of tomorrow's genome is discussed in chapters on the fields of cancer (Cavenee and Georgiev), sequence analysis (Cantor), and in the increasingly important field of plant biotechnology. I found Cantor's chapter on DNA sequencing beyond the genome project particularly interesting. He has some interesting thoughts on how we will identify new genes or perform diagnostics, evolutionary studies, and expression screens when the completed human sequence is available. Will we be using DNA as an additive, rather like an invisible bar code, to tag medicines or samples for which we will subsequently have the ability to screen for authenticity. Is the future really based in chips with everything?

The order of topics in the book is progressive with an overall trend of moving down the hierarchy of structure from chromosome to sequence and then to applications of this technology. They carry the reader along, but by no means preclude one from dipping into a favourite area as each chapter stands alone on its own merit. It is refreshing to have a book on chromosome and chromatin analysis, with a broader view of the field. One only has to note the increasing interest in the field owing to new molecular insights in the field of epigenetics and genome partitioning to appreciate the resurgence of this area of research. As such, the broader feel to this makes it an excellent text for more advanced students of the field who want to widen their horizons.

As to the style of the book, it has to be said that there is little cross referencing between chapters and the index is adequate rather than extensive. The references for each chapter again range from good to excellent, but are more than adequate launching points into other publications. I was initially somewhat worried when the opening chapter launched in at the very deep end with detailed experimental procedures and its emphasis on technical aspects of chromatin and chromosome analysis. However, subsequent chapters achieve a good balance between technical and review styles. The book more than lives up to its promise. Within its rather ordinary cover lie interesting tales of how today's genome is gradually becoming understood as multiple layers of interlocking functional environments. What is more, it throws in some hints about what tomorrow's human genome sequence might have in store for us. Somehow, I think that the completed sequence will just be the beginning, a start for integrative functional studies addressing whole genome function.

MARK C HIRST

Culture, Kinship and Genes. Editors Angus Clarke, Evelyn Parsons. (£45.00.) UK: Macmillan. 1997. ISBN 0-312-17499-3.

Genetic counselling "consists largely of talking", says Angus Clarke in the introduction to this volume. Through it, a person, couple, or family at risk of developing or