Book reviews

Lupus. Molecular and Cellular Pathogenesis; Edited by G.M. Kammer and G.C. Tsokos, Humana Press; Totowa, New Jersey, 1999, xx+708 pp. $ 195.00 (hb). ISBN 0-896-03556-5

Owing to its status as a prototypic autoimmune disease, systemic lupus erythematosus (SLE) has attracted the interest of a broad spectrum of basic as well as clinical scientists in the past. Arguing that no single unified hypothesis on the etiopathogenesis of lupus has emerged, the editors of the present volume released by Humana Press aim to provide a comprehensive overview of current basic lupus research at the cellular and molecular levels.

The authors of each chapter have been asked specifically to outline their working hypothesis and to discuss future directions in their respective research areas over the next few years. The book encompasses 40 chapters including brief descriptions of the clinical entity and current therapeutic options. The particular virtue of this book is, however, that it puts together a wide selection of recent basic research pertinent to lupus thereby establishing a valuable source of inspiration for interdisciplinary research in this elusive disease. The panel of authors is both eminent and diverse, reflecting the many distinct issues which have to be addressed to cover the subject in depth.

The significance of genetic and environmental factors in the causation of triggering of lupus is discussed in detail. It is rightly emphasized that a discordance rate amounting to 70% among monozygotic twins strongly suggests a role for exogenous agents. The significance of as yet unidentified 'SLE viruses' or infection of genetically susceptible hosts by commonly occurring viruses is thoroughly outlined with particular emphasis on retroviruses, Sinbis virus and Epstein–Barr virus. A chapter is devoted to a review of vascular endothelial cell function which is of key interest not only in the context of lupus-related vasculitis but also with respect to premature atherosclerosis which has become a major cause of late morbidity and increased mortality among long-term lupus survivors. The chapter on T-cell subpopulations pays particular attention to the possible significance of defective type I protein kinase activity as a cause of impaired antigen-stimulated cell activation. DNA hypomethylation in T-cells is presented as another potential mechanism behind autoreactivity based on observations in lupus-like disease in animals. Evidence is referred to suggesting that disease exacerbation is associated with increased production of B-cell stimulatory cytokines, e.g. induced by exposure to environmental factors like certain drugs.

The complement system and its significance in SLE are elegantly reviewed with particular emphasis on complement as a double-edged sword facilitating proper immune complex processing and at the same time contributing to tissue damage.

Taken together, the editors and the authors should be congratulated for having managed to compile and present such a treasury of updated research results from cell biology, biochemistry and molecular genetics focused on SLE. This book is equally valuable to clinicians and scientists engaged in lupus research. A follow-up edition dealing with the many issues and questions raised in this volume will be welcomed by lupologists worldwide.

Peter Junker

Mitochondria; Edited by I.E. Scheffler, Wiley; Chichester, 1999, xiv+367 pp. £ 64.50 (hb). ISBN 0-471-19422-0

Mitochondria have gained a new wave of interest over recent years in medical sciences as well as in other fields. The main reason for this is the recognition of major roles of these organelles in diseases such as cardiomyopathies and neurodegenerative disorders, developmental processes such as apoptosis, cancer, ageing and male sterility in plants. Thus, not only students but also a growing number of mature investigators will discover or rediscover mitochondria and will appreciate getting extensive information on all topics concerning mitochondria in a single source of information.

This unique one-author book covers all aspects on mitochondria ranging from biochemistry, biophysics, and cell biology, to diseases, evolution, anthropology, genetics, forensics, and others. It is written in such a comprehensive way that it can be considered not only a textbook, but much more. Each chapter reads like a fascinating novel, with historical perspectives, debates, challenges, conceptual and technical limitations over the years, emphasis on the progression of the knowledge, interesting overviews as well as sufficient detail and depth on the present-day situation for each topic. Moreover, a number of unsolved problems are often listed so as to stimulate the imaginative power of the reader! Bibliographic citations have been selected with much scrutiny and key references are annotated so that this book can really be considered a "convenient springboard into the voluminous past literature, as well as future publications", as suggested by the author. In the illustrations, colored crystallographic structures of respiratory chain complexes are much appreciated.

The book is divided into nine chapters. Chapter 1 recalls the history of the discovery of mitochondria as well as the main milestones along the way of understanding mitochondria. Chapter 2 discusses the evolutionary origin of mitochondria including the various theories, their weaknesses and strengths. The extensively illustrated Chapter 3 is devoted to structure, morphology and integration into the cell. Then follows the most important chapter (spanning one third of the book), devoted to biogenesis. This chapter deals with the mitochondrial genome in various organisms, nuclear genes encoding mitochondrial proteins, replication, transcription, translation, protein import, and protein degradation within mitochondria. A detailed state-of-the art description of mitochondrial electron transport and oxidative phosphorylation is presented in chapter 5. This chapter first recalls the technical difficulties encountered in studies of the electron transport chain and some challenging solutions to these problems, as well as a detailed analysis of each complex. Then alternative pathways for electron transport in other organisms are presented followed by a strong review of the chemiosmotic hypothesis and a detailed description of ATP synthase. The chapter ends with a discussion on the control of respiration and oxidative phosphorylation, the fate of reactive oxygen species and the role of specific lipids. Chapter 6 is about the metabolic pathways inside mitochondria, including not only the most classical Krebs cycle, fatty acid degradation and urea cycle but also biosynthesis of heme, of ubiquinol and of cardiolipin. Chapters 7 and 8 are devoted to mitochondrial mutations and disease as well as to polymorphism of mitochondrial DNA and its relationship with anthropology. These fascinating chapters review the knowledge on mutations in mitochondria from various organisms, the molecular genetics of human mitochondrial diseases, the relationship between mutations and ageing and the link with apoptosis. Finally, the powerful use of mitochondrial DNA sequencing in human and primate evolution is described as well as potential forensic applications and future challenges. The very last three-page chapter 9, entitled 'Mitochondria and pharmacology', lists a number of drugs and inhibitors which are useful in the study of mitochondria.

All along, the prospective view of the author ("on whom the subject has grown over the years") recalls how the fascinating mitochondria have been pivotal in the development of some of the most profound ideas in modern biology. Moreover, it shows how they are intimately linked to fundamental biological questions about energy production in the basic unit of life, about health and disease, evolution of humans and other organisms.

Catherine Florentz

0014-5793/01/$20.00
PII: S0014-5793(01)02307-9

Nuclear Receptors. A Practical Approach; Edited by D. Picard, Oxford University Press; Oxford, 1999, xviii+285 pp. £ 31.95 (pb). ISBN 0-19-963742-3

This volume from the Oxford University Practical Approach series is comprised of 11 chapters and is edited by an active and innovative contributor to the field. Most chapters start with a short introduction which provides useful background information to newcomers in the field. The protocols are comprehensible and alternative protocols allow more flexibility in the choice of the appropriate method. The first two chapters describe the nuclear receptor superfamily and explain how to clone and characterize new receptors. The following chapter shows how to identify the ligands and provides protocols for transactivation and ligand binding assays and for monitoring changes in the conformation of receptors. Additionally, the reader gets advice about how to perform a coactivator-dependent receptor ligand assay and fluorescence spectroscopy. Chapter 4 describes the kinetic analysis of receptor interactions and covers both protein–protein interaction and DNA–protein interaction. Then, the reader is guided through the functional characterization of coactivators using mammalian cell microinjection. In the next chapter, the identification of phosphorylation sites in nuclear receptors, the identification of candidate kinases and the functional significance of phosphorylation are discussed. Chapter 7 focuses on ligand- and cofactor-regulated transcription and covers the purification and analysis of recombinant receptors and cofactors, in vitro chromatin assembly and in vitro transcription. Methods for the analysis of hormone resistance syndromes are explained in chapter 8. Receptor analysis, ligand and DNA binding studies and assays of mutant receptor function are also covered in this chapter. The next chapter described the in vitro assembly of receptor–HSP90 complexes and the analysis of assembly reactions. Chapter 10 is dedicated to approaches and techniques that use yeast as a model system for investigating nuclear receptor function. The final chapter covers the regulation of heterologous proteins by fusion to the hormone binding domain of a receptor.

In summary, this book is a comprehensive collection of relevant methods that is helpful for both basic and clinical researchers. It provides information on how to study the steroid/nuclear receptor superfamily which plays a major role in a variety of physiological and pathological processes. *Nuclear Receptors. A Practical Approach* gives background information combined with precise practical hints and tips provided as annotations in the protocols. The organization of the chapters is excellent. The schematic depictions of the protocols are helpful to understand the principles of the methods. Additionally, the summaries of the required equipment and reagents at the beginning of the protocols are useful for planning the experiments. Furthermore, advantages and disadvantages of different methods are discussed. However, the book would benefit from a troubleshooting section in each chapter.

In conclusion, this is a book that is highly recommendable and is a successful approach to answer many theoretical and practical questions that may arise in research laboratories that are working in this complex field.

Stefanie Denger

Cell–Cell Signaling in Bacteria; Edited by G.M. Dunny and S.C. Winans, Blackwell Science; Oxford, 1999, xi+367 pp. £ 59.00 (hb).

This is a wonderful book that compiles a series of reviews that summarize the current state of prokaryotic cell–cell communication. The book is organized into five parts, each focusing on a common biological theme. This organization provides an excellent context for examining how different groups of bacteria approach common problems by a variety of mechanisms. Each chapter provides a clear and comprehensive review of each specific topic and relates the topic to the overall theme. The book covers a wide spectrum of prokaryotic signaling systems including multicellular development in Gram-negative and Gram-positive bacteria, bioluminescence, peptide pheromones, acylated homoserine lactones, and pathogenesis, to name just a few. While it is impossible to cover all aspects of prokaryotic cell–cell signaling the editors have compiled an excellent collection of reviews that covers the diversity of this field very well. In particular, the introductory chapter by Dunny and Winans provides an interesting historical perspective to the topic of prokaryotic cell–cell signaling and provides a general introduction to the various systems and themes that are presented in the book. This sets the stage for a detailed analysis and review of the various topics that follows. Finally, Dunny and Winans provides an answer to one of the most basic questions concerning the field of cell density communication, what is the genesis of the term 'quorum sensing'.

Part I comprises five chapters devoted to cellular communication for the purpose of genetic transfer and development. The link between these two processes may not be obvious at first; however, Chapter 3 on *Bacillus subtilis* quickly reminds the reader of the intimate coupling between developmental sporulation and gene transfer. Of the five chapters in part I, two are devoted to two different and independent cellular signaling systems in the Gram-negative social bacterium *Myxococcus xanthus*, the A-signaling cell density system, and the cell contact system, known as C-signaling. Both signaling systems play important roles in the developmental process of the *M. xanthus*. Two chapters are also devoted to genetic transfer in Gram-positive bacteria. Chapter 2 discusses the role of the competence peptide pheromones in *Streptococcus*; and chapter 4 reviews the role of the peptide pheromones in plasmid conjugation in *Enterococcus*. This is an interesting system, since the recipient strain produces the pheromone to promote plasmid transfer from the donor. The keystone to part I is chapter 3, which ties together the theme of genetic transfer and development, by reviewing the work on the *B. subtilis* cell density pheromones that modulate both competence and sporulation.

Part II is devoted to symbioses, and includes four chapters covering both plant–microbe and animal–microbe associations. Chapter 7 provides an excellent introduction to this topic by providing an overview of the autoinducers, *N*-acyl-homoserine lactones, a family of compounds used as signaling molecules in a variety of Gram-negative bacteria. The regulatory role these signaling molecules play in a variety of cellular interactions is discussed. Chapter 10 continues on the theme of how *N*-acyl-homoserine lactones are used as autoinducers to regulate gene expression. This chapter details the complex role of this signaling molecule in the human pathogen *Pseudomonas aeruginosa*, and the identification of two independent autoinducing systems. A discussion of *Agrobacterium tumefaciens* and a review of Ti plasmid infection of plant cells and its regulation follow. The final chapter in part II is a review of the pathogen *Staphylococcus aureus* and its use of peptide-based density signaling.

The regulation of the production of antimicrobial compounds is the focus of part III. Three chapters discuss how cell–cell signaling regulates a variety of antimicrobials including the lantibiotics, small antimicrobial peptides produced by a variety of Gram-positive bacteria; the peptide bacteriocins from lactic acid bacteria; and a variety of secondary metabolites, many of which have antimicrobial activity, from *Streptomyces* spp. Though each chapter outlines the background and importance of the antimicrobials being discussed, the bulk of the review focuses on the regulation and the control of production by cell-derived signals.

Part IV, 'Molecular basis of cell–cell signaling', comprises five chapters that specifically examine the molecular mechanisms of signal generation, signal reception, and gene activation. Four of the five chapters specifically examine the role and mechanism of how different Gram-negative bacteria produce and respond to *N*-acyl-homoserine lactones, while the fifth chapter examines the role of peptide pheromones and their role to modulate the developmental process in *B. subtilis*. Chapter 14 is an excellent review and discussion of *N*-acyl-homoserine lactones. It provides an in-depth comparative analysis of the variety of structures that comprise this class of signal. It also

provides a detailed analysis of the enzymology and biochemistry of the production of the class of signal molecules. Chapters 15 and 17 examine how cells respond to the autoinducers, by examining the mechanism of autoinducer reception and activation of gene expression. In both cases, the LuxR–LuxI system is used as the model. What is of interest is how complex the systems can become from one organism to another. In chapter 17, the emphasis is on *Vibrio harveyi*, which uses a dual production and response system to regulate bioluminescence. My only disagreement with the editors is that this chapter should have followed Steven and Greenberg's chapter. The intervening chapter by Pergo is an excellent review of peptide signaling and its role as a modulator of sporulation initiation in *B. subtilis*.

The final section of this volume, Part V, 'Past and future', contains four chapters ranging from a historical account of quorum-dependent gene expression to a general discussion on the role of quorum sensing in natural populations. Once again, the role of *N*-acyl-homoserine lactones is the major focus.

Overall, this is an excellent book dedicated to understanding of how bacteria communicate with each other to perform a wide variety of tasks, including coordinating multicellular development, controlling bioluminescence, pathogenesis and production of secondary metabolites. The book reviews a variety of different systems and puts them into larger biological context. It is an excellent resource for anyone interested in the field of microbial communication.

Mitchell Singer

Chemokines in Disease: Biology and Clinical Research; Edited by C.A. Hébert, Humana Press; Totowa, New Jersey, 1999, xx+330 pp. 150.00 (hb). ISBN 0-896-03703-7

The initial identification of a small number of *chemo*tactic cyto*kines* (chemokines) offered the promise of understanding how specific leukocyte subsets are recruited to areas of inflammation. In an almost unprecedented tour de force, laboratories from around the world have recently characterized over 40 chemokines and 17 chemokine receptors. This large number of chemokines and chemokine receptors, many with overlapping functions, has resulted in confusion regarding the role of chemokines in health and disease. In particular, many investigators have expressed concern that a functional redundancy exists which could diminish the therapeutic utility of blocking a single chemokine or chemokine receptor in the treatment of inflammatory disease. The timely publication of *Chemokines in Disease* relieves much of this confusion through the elegant compilation of data demonstrating the functional relevance of chemokines in disease pathogenesis.

This volume is divided into four sections. The first two sections detail the discovery of novel chemokines, and then examine the pro-inflammatory role of what may be considered 'classic' chemokines (e.g. IL-8, MCP-1, eotaxin, RANTES, MIP-1α, and MIP-1β). The final two sections demonstrate the diversity of chemokine function by reviewing the relationship of chemokines to cell proliferation and cancer, and the opportunistic manipulation of chemokines and chemokine receptors by viruses. Each chapter resembles a review article, and can stand on its own. The chapters are well referenced, having been written by leaders in the field of chemokine biology. This book is very readable, and provides an excellent introduction to chemokines for investigators from other fields, as well as a comprehensive reference source for scientists familiar with chemokine biology. Although discussed throughout the book, including an initial chapter dedicated to the classic chemokines would have been useful, especially for those unfamiliar with this field. Because chapters are structured as review articles, there is some repetition, especially in the introductory material, which generally provides an overview of chemokines and chemokine receptors. This is a necessary sacrifice if each chapter is to be self-contained. The text contains many typographical errors, and some of the figures are truncated, but generally these are minor annoyances.

In a text of this quality it is perhaps arbitrary to single out specific chapters as highlights; however, I have chosen one chapter from each section to illustrate the depth of the work presented in this volume.

In chapter 4 Boring et al. describe the compelling evidence that MCP-1 has a non-redundant role in recruiting leukocytes to areas of inflammation or injury. The authors consider data from MCP-1 neutralization studies, mice that overexpress MCP-1, and mice that do not express MCP-1, or its receptor CCR2. In addition to describing the results of such experiments, the data are interpreted, and when appropriate the authors provide alternative hypotheses to fit the data. The difficulty with considering MCP-1 primarily as a regulator of Th2-specific responses is nicely discussed and supported through data from the CCR2 knockout model.

In chapter 6, Martin and Goodman present an exhaustive discussion of studies that examined chemokines in human acute respiratory distress syndrome (ARDS). They offer these correlative data as hypothesis generating, and point out the direction research needs to go to prove a relationship between chemokines and ARDS. The problems encountered with existing methods of sampling alveolar fluid for chemokine expression are highlighted and used to explain discrepant results from different studies. Finally, the authors outline the pros and cons of inhibiting CXC chemokines such as IL-8, GRO, or ENA-78, or blocking the chemokine receptors CXCR1 and CXCR2 in the treatment of ARDS.

In chapter 14, Czaplewski et al. explore the use of an engineered variant of the CC chemokine MIP-1α to inhibit hematopoietic stem cell proliferation as a means of protecting bone marrow and enhancing recovery during cytotoxic chemotherapy. The requirements for using variant MIP-1α as a clinical therapeutic agent are described, and the results of phase 1 and phase 2 clinical studies are presented. The evidence that variant MIP-1α conferred a significant protective effect in these trials is not overwhelming. However, this chapter does provide an excellent illustration of a potentially novel, non-inflammatory function for chemokines. In another example of how the chemokine system is involved in non-inflammatory settings, Berger and Farber (chapter 15) offer a historical perspective on the discovery that the chemokine receptors CXCR4 and CCR5 may function as HIV co-receptors. These authors also discuss other chemokine receptors that may have co-receptor activity, and describe the genetic evidence from studies of a CCR5 polymorphism that establishes a role for this receptor in HIV disease. This lucid chapter provides a foundation for understanding the potential for development of HIV therapeutics based on the principle of chemokine receptor antagonism.

In summary, this is a text that one can read cover to cover in a reasonable period of time to obtain a concise overview on the diverse biology of chemokines and chemokine receptors. It puts many of the issues raised with the discovery of this large cytokine family into perspective, and presents a direction for future chemokine research. On a second level, each chapter provides details useful to investigators requiring more than a casual assessment of the field. *Chemokines in Disease* should be welcomed into the libraries of a diverse audience, including those interested in inflammation, oncology, and virology.

Brad H. Rovin

Prokaryotic Gene Expression; Edited by S. Baumberg, Oxford University Press; Oxford, 1999, xx+325 pp. £ 32.95 (pb). ISBN 0-19-963603-6

In the past 20 years it has become increasingly evident that prokaryotic gene expression is no longer of only academic interest. The rapidly increasing knowledge of regulatory mechanisms underlying bacterial gene expression has paved the way for modern biotechnology and may in the future have important implications for antibacterial drug design.

The book starts with a historical overview written by the editor S. Baumberg, in which he briefly summarizes the key discoveries in and the main topics of bacterial gene expression. Since gene expression is an interplay between proteins and nucleic acids, the second chapter is devoted to protein recognition of specific sites in DNA and RNA. This section illustrates nicely how repressor proteins recognize DNA and how end products and inducers result in repression or induction of certain gene clusters. The next two chapters deal with transcription including different promoters, sigma factors, polymerases, and transcriptional activation and repression. Both chapters provide a comprehensive overview of the topic as well as a deeper insight into the molecular mode of action of selected regulatory proteins.

The following chapter covers most of the important regulatory mechanism operating at the post-transcriptional level including mRNA stability and decay, translational repression, antisense mechanisms, frameshifting, translational introns and mRNA recoding. Given the steadily increasing importance of post-transcriptional regulatory events in bacterial gene expression, the book would have deserved additional chapters dealing with various aspects of this topic in more detail.

In the following chapters, gene regulation is viewed in terms of environmentally controlled regulatory networks starting with the implications of DNA topology on gene expression. The function of enzymes and proteins affecting the structure of the bacterial nucleoid is discussed. Next, the global regulatory network governed by sigma-S is described. This section covers parameters affecting sigma-S synthesis and stability, and deals with genes and their function regulated by sigma-S. Then, bacterial signal transduction systems known as two-component systems are reviewed. The authors highlight the commonalties of these systems as well as their diversity and flexibility. Next, genetic switch systems are described and well exemplified for several pathogenic bacteria. This chapter covers strand slippage mechanisms, phase switching by DNA inversion and variation by homologous recombination.

The last two chapters deal with complex regulatory networks governing the expression of virulence factors in pathogenic bacteria as well as spore formation and the production of antibiotics. The regulatory cascades regulating virulence gene expression are discussed for several pathogens of animals and humans as well as for the plant pathogen *Agrobacterium tumefaciens*. The regulatory devices operating during spore formation in a single *Bacillus* cell and during multicellular differentiation which leads to spore formation in *Streptomyces* spp. again nicely demonstrate the complexity of these developmental processes. Finally Baumberg remarks on the evolution of prokaryotic regulatory systems with the notion that in the prokaryotic world distinct regulatory pathways lead to the same or a similar outcome in different bacterial species. This short summary certainly shows that a lot has to be learned for a better understanding of why and how this diversity has evolved.

In summary, the book provides an excellent synopsis of the key topics in prokaryotic gene expression and can certainly be recommended for advanced graduate students in the field. In addition, the book provides a good source for lecturers in the field. A shortcoming of the book is the rather small number of illustrations.

U. Bläsi

Peptide Nucleic Acids; Edited by P.E. Nielsen and M. Egholm, Horizon Scientific Press; Norfolk, 1999. x+266 pp. £ 59.99 (hb). ISBN 1-898486-16-6

Peptide nucleic acids (PNAs) are DNA mimics whose structure and unique properties were first described in 1991 by P. Nielsen, M. Egholm and colleagues. The molecules were originally designed as ligands for the recognition of double-stranded DNA. They have been extensively studied since then in several laboratories, and their unique chemical, physical and biological characteristics have been exploited to produce biomolecular tools, molecular probes, biosensors and antisense and antigene agents.

The book is a collection of established techniques and protocols using PNAs. The information is clearly given, with each chapter taking the form of a short paper. Each method is presented in a clear, step-by-step manner together with appropriate results and discussion. Moreover, each chapter concludes with a comprehensive list of reference articles. The volume is divided into five sections: introduction, chemistry, hybridization-based techniques, biomolecular tools, and antisense/antigene technology, for a total of 20 chapters written by 45 authors. The editors, P. Nielsen and M. Egholm, have done a first-rate job in bringing together excellent subject matter written by recognized scientists in the field of PNAs.

The first chapter provides an extensive introduction to PNAs, describing their structure and properties and some of the most common applications. The following five chapters are devoted to the chemistry of PNAs: two of them describe the synthesis of PNAs by Boc and Fmoc chemistry, two other chapters deal with PNA–DNA chimeras and the chemical strategies for their synthesis. Such chimeras, which result from the combination of PNA and DNA into one molecule, are characterized by biological properties distinct from those of PNAs, such as the ability to serve as primers for DNA polymerases and to stimulate cleavage of the target RNA by RNase H upon the formation of an RNA–chimera complex. Another chapter describes the procedures currently used for radioactive and non-radioactive PNA labeling.

Six chapters are devoted to hybridization-based techniques. The first one is focused on the thermodynamic properties of PNAs and their complexes with nucleic acids and introduces the use of absorbance melting curves for the determination of thermodynamic parameters of PNA hybridization. Another chapter provides an overview of established protocols for in situ hybridization using PNA probes in histochemistry, fluorescence microscopy and flow cytometry and gives a number of possible applications. The third chapter deals with the use of PNA oligomers in array technology (DNA chips) for the analysis of nucleic acids and describes means and procedures for the in situ synthesis of PNA arrays on membranes. This is an important issue, since, due to the unique features of PNA–DNA interaction, the use of arrayed PNA oligomers could offer superior hybridization features compared to conventional oligos. The fourth chapter discusses the possibility of enhancing specificity in probe assays by the use of PNA blocker probes that prevent the mismatch hybridization of detector probes to non-target sequences. Another chapter describes an interesting approach for the detection of single nucleotide polymorphisms in DNA by employing allele-specific PNA hybridization probes and analysis by MALDI-TOF mass spectrometry. The last chapter reviews the use of PNA as a novel probe for sequence-specific biosensors, gives common PNA biosensing protocols, and discusses their perspectives in DNA biosensor technology.

The fourth section of the book includes four chapters describing the great potential of PNAs for use as tools in biotechnology and molecular biology. In the first chapter, the PARC (PNA-assisted rare cleavage) technique is described, and data are presented to demonstrate that by combining bis-PNA with methylases and frequently cutting restriction endonucleases it is possible to generate a new class of genome rare cutters that allow cleavage of whole DNA into a limited number of pieces. The possibility of isolating and purifying specific double-stranded DNA sequences by oligonucleotide/PNA-assisted affinity capture is another interesting application of PNAs described in the book, as is the use of affinity-tagged PNA capture probes for the

purification of nucleic acids by hybridization. PNAs are also used in the PCR clamp method for the detection of single basepair mutations in DNA for the diagnosis of genetic diseases. Again, labeling plasmid DNA with a fluorescent PNA, without affecting its ability to be efficiently transcribed, is a valuable method to follow the delivery of DNA in cells.

In the fifth section of the book, the role of PNAs as lead compounds for the development of gene-targeted drugs by applying antigene or antisense strategy is discussed. One chapter details with methods for testing the antisense activity of PNAs in *Escherichia coli*. By virtue of their ability to form strand displacement complexes with double-stranded DNA, PNAs are capable of arresting transcriptional processes. One chapter carefully describes the background, protocols and limitations of the molecular biology and enzymatic methods currently used to examine PNA/DNA strand displacement complexes. In the last chapter of the book, protocols using PNAs for studying the activity of enzymes that interact with DNA are given. Specifically, the possibility of inhibiting human telomerase by the use of PNAs complementary to its RNA template is clearly described, together with the use of PNAs for probing substrate recognition by helicases.

At the end of the book there is an appendix which provides guidelines for the sequence design of PNAs, information for handling and storage, and useful technical suggestions for their correct use in experiments.

Unfortunately, the problems related to the delivery of PNAs to intact cells are not addressed in the book. The cellular uptake of PNAs is very slow and limited, and it is considered to be the major challenge that must be overcome before PNAs can be used in vivo. The point should have been discussed in the book in light of recent progress in the area. In fact, in the last few years, efforts have been made by investigators to increase the cellular uptake of PNAs by modifying the molecule itself or conjugating it to ligand molecules or internalization peptides that could enhance a physical or receptor-mediated cellular uptake.

In summary, the book provides an excellent source of information for individuals who are interested in PNAs. It is comprehensive and accessible, since, at least for many chapters, it does not assume much previous knowledge. It will thus be valuable not only to experts in the field but also to first-time PNA users.

Nadia Zaffaroni

Encyclopedia of Molecular Biology (4 volume set); Edited by T.E. Creighton, Wiley; Chichester, 1999, xix+2856 pp. £ 795.00 (hb). ISBN 0-471-15302-8

Magisterial, massive, monumental···. These are all adjectives appropriate to this huge undertaking, created by over 400 contributing authors, with 2000 topic entries, and edited by Thomas E. Creighton.

It is one of four biotechnology encyclopedias with Leroy Hood as Series Editor, aided by a distinguished Editorial Board. Hood contributes a preface, but not Creighton.

Without an introduction for guidance, we are left to open the pages, sample the contents and get a feeling for how useful this compendium will be.

What kinds of articles? All carry attributions. All but the shortest (from one paragraph to 17 pages) have a bibliography of from a few to 100 or more citations. When one concentrates on the longer articles, it is like feasting on a surfeit of 'Trends' reviews. They are authoritative, well-illustrated (monochrome) and with the occasional 1999 citation. (The citations peak around 1996.)

How comprehensive? One suspects that every effort has been made in this respect, but this aspect cries out for a statement of intent from the Editor. The index does not help. It is very inadequate. For this biased reader, it was disconcerting to find that while glycogen degradation and glycogen phosphorylase (four pages) were included, glycogen synthesis and glycogen synthase were not. The limitations of the index may be judged by the relative paucity of entries. A biochemistry textbook taken from the shelf (Voet, Voet and Pratt) has more than three times as many entries on a per page of text basis as does Creighton, 7.6 vs. 2.4. Yet my feeling is that the longer the text, the greater should be the density of index terms, not lower.

For something as extensive as this, a useful feature to have added at the front would have been a list of long entries, as in Kendrew's 1994 one-volume work of the same title.

Short of a detailed, systematic search, one has to take it on trust that the subject coverage is adequate, but if this is to be used for quick and ready reference, the user is likely soon to become frustrated. Here is a random sample of entries from the Kendrew encyclopedia that are missing from Creighton, being neither in the index nor as an entry of that name: lysosome, platelet-activating factor, molecular biology, (cell) motility, leucocyte, gonadotropins, dopamine, opiate receptors, gene therapy, patch clamp, protein phosphatase, genetic engineering.

Southern blotting is an entry, but is not indexed. And with all these lacunae, 4.5 pages on ornithine decarboxylase, to which Kendrew does not devote a single word.

This encyclopedia is a tantalizing compilation. It may be likened to the curate's egg. It surely has rich treasures in store for those who persist and burrow beneath the surface. It is a long and worthwhile journey through molecular biology that is flawed for lack of an adequate road map.

William J. Whelan

Free Radicals. Biology and Detection by Spin Tapping; Edited by G.M. Rosen et al., Oxford University Press; Oxford, 1999, xii+482 pp. £ 65.00 (hb). ISBN 0-19-509505-7

This work apparently started out as "a modest sized handbook on spin trapping" (page vii), to which became added a general account of free radicals in biological systems. In fact the bulk of the book is still devoted to spin trapping, and that is what most readers will look to this book for. Nevertheless, chapter 1 gives a concise but thoughtful and readable account of how O_2 affected the evolution of life on the earth. Chapter 2 ('the oxygen paradox') is a brief but accurate discussion of O_2 toxicity and antioxidant defences including a good summary of the role played by iron in free radical damage. Chapter 3 attempts to do the same for nitric oxide, although the discussion of $ONOO^-$ seems somewhat dated. So many books and reviews have been devoted to NO recently that it is difficult to say anything new.

Chapter 4 discusses 'methods of free radical detection' and has a good summary of the artefacts in the various methods that have been used to detect $O_2^{\bullet-}$ and $OH^{\bullet}$, but is less analytical about the equally flawed techniques used to measure H_2O_2. It leads on to the 'meat' of the book: the use of spin-trapping. The history of the technique is briefly covered; subsequently chapter 6 details the methods used to synthesize spin traps, including isotopically labelled and phosphorylated ones. Chapter 7 explains the principles of ESR, and chapter 8 reviews the kinetics of spin trapping free radicals (especially $O_2^{\bullet-}$ and $OH^{\bullet}$), an understanding of which is essential to comprehend what is likely to happen when this technique is applied to complex biological systems. As Perkins et al. wrote in 1980, "Failure to observe a spin adduct does not prove the absence of radicals". Reading pages 362 onwards makes one aware that the opposite is also true, that spin adducts can readily be generated artefactually. I was surprised not to

see more attention given to the reduction (chemical or otherwise) of spin adducts by biological systems, which has probably confused many experiments. Another area of confusion has resulted from the use of impure traps purchased commercially.

If spin traps intercept a significant percentage of the free radicals formed in a system, and if these free radicals cause damage, then the spin trap ought itself to exert an antioxidant protective effect. Chapter 10 reviews the evidence for this, but makes it clear that many spin traps have additional mechanisms of action. Whether spin trap-based drugs will turn out to be therapeutically useful remains to be seen.

Overall, an excellent book. Read it to find out all you need to know about spin trapping oxygen radicals.

Barry Halliwell

Rotaviruses. Methods in Molecular Medicine; Edited by J. Gray and U. Dresselberger, Humana Press; Totowa, New Jersey, 2000, x+262 pp. $ 89.50 (hb). ISBN 0-896-03736-3

Volume 34 of the series 'Methods in Molecular Medicine' covers most aspects of the modern experimental procedures developed in studies of rotavirus (RV) pathogenesis. Moreover, some chapters cover several clinical aspects of RV infection including epidemiology and vaccinology. The book is well written and easy to read. In general, the clarity and organization of the chapters are excellent. The chapters are structured in a consistent way containing (i) an introduction to the relevant particular subject including the description of the methods needed for the specific objectives, (ii) a list of equipment and reagents needed, (iii) methods with detailed protocols for their adequate use and for some of them illustrations were included to show results obtained, (iv) notes with advice, hints, trouble-shooting and comments on choices, (v) a list of references.

All 12 chapters are written by experts in the fields, some of whom have played a direct role in the advances in RV pathogenesis and/or the development of a particular technique. Chapter 1, written by U. Desselberger, entitled 'Rotaviruses: Basic facts', gives a general introduction on the different aspects analyzed in the book, which are further detailed in the specific chapters. Chapter 2, written by B.V. Venkataram Prasad and M.K. Estes, entitled 'Electron cryomicroscopy and computer image processing techniques', gives a pertinent and well documented analysis of the current knowledge of the molecular organization of RV. Figures included in this chapter showing 3D reconstructions give a comprehensive description of how the RV structure is organized. Chapter 3, written by J.T. Patton, V. Chizhikov, Z. Taraporewala and D. Chen, entitled 'Virus replication', completes appropriately the preceding chapter, by giving technical procedures needed to study the RV genome, the assembly and structure of rotavirion, and the structure of RV proteins. Moreover, this chapter contains a lot of detailed and helpful methods for isolation of RV proteins and particles, illustrated with appropriate figures showing results obtained – a chapter organized as it should be for a laboratory manual. Chapter 4, written by M. Gilbert and H.B. Greenberg, entitled 'Rotavirus entry into tissue culture cells', and chapter 5, written by R.F. Raming, entitled 'Mixed infections with rotavirus', describe different protocols for cell infection by RV and virus-like particles. Although well written, documented and illustrated, these chapters describe only the non-polarized fetal African green monkey kidney cell line MA104 as a cellular model for RV cell infection. Unfortunately, this cell line does not currently represent the unique cellular model to study RV cell infection. In particular, MA104 cells are not appropriate to study different aspects of RV cell pathogenesis in the laboratory. Indeed, it is well established that RV infects preferentially the mature enterocytes of the small intestine which are polarized. In consequence, the unpolarized MA104 cells do not allow studies on polarized cell entry and intracellular trafficking, cellular responses, and structural and functional consequences of the RV infection. Chapter 6, written by L.S. Saif and L.A. Ward, entitled 'Pathogenesis and animal models', reports on the use of gnotobiotic pigs in RV research. Other animal models, such as gnotobiotic rats and mice that are more easily used than the pig model to study RV infection in the absence of microflora and with complementation with human microflora, have not been described. The interest of this chapter is limited, although it contains technical procedures on histological, immunochemistry and immunofluorescence methods. Chapter 7, written by K.K. Macartney and P.A. Offit, entitled 'Immunologic methods and correlates of protection', chapter 8, written by M.A. Franco, entitled 'In vivo study of immunity to rotaviruses', and chapter 9, written by M. Ciarlet and M.E. Conner, entitled 'Evaluation of rotavirus vaccines in small animal models', represent a set of comprehensive information on the immune response to RV infection in human and animal models, and on the evaluation of RV vaccines in animal models. Chapter 9 offers particularly substantial helpful and detailed information on the techniques, protocols and methods previously used by research workers to conduct experiments in vaccinology in animal models. Chapter 10, written by M.I. Gomara, J. Green and J. Gray, entitled 'Methods of rotavirus detection, sero- and genotyping, sequencing, and phylogenetic analysis', describes the laboratory procedures, including electron microscopy, biochemical methods, or RT-PCR necessary to examine clinical RV infection. Chapter 11, written by M. Ramsay and D. Brown, entitled 'Epidemiology of group A rotaviruses', describes the epidemiological features of group A RV infection, and gives a critical review of the current surveillance strategies used to define the burden of disease. The last chapter, written by U. Desselberger and M.K. Estes, entitled 'Future rotavirus research', appropriately completes the book by the inclusion of some new insights obtained in experimental studies on RV pathogenesis and gives pertinent commentaries on current clinical studies, particularly those concerning the recent setback that has refocused attention on RV vaccines.

In conclusion, *Rotavirus – Methods and Protocol*, which gives an overview of RV research, is a recommendable comprehensive guide for practice by research workers and graduate students in the field of virology and infectious diseases. However, I am afraid that chapters 4 and 5 focusing on RV cell infection are currently not as useful as analyzed above. During the past 10 years, cellular microbiology had benefited from the development of appropriate cellular models to give new insights into the microbial pathogenesis of enterovirulent microorganisms. Currently, the human adenocarcinoma cell lines that mimic in culture the mature enterocytes of the small intestine are a more appropriate model than MA104 cells to investigate pertinently the cellular impact of RV infection. In the future, a chapter focused on the description of such cell lines would certainly strengthen the book. Additionally, it should describe the general biochemical and biophysical methods used to study the organization and functionality of polarized cells. This chapter may be useful for research workers for whom the objectives are to study the cellular and molecular mechanisms of RV pathogenesis, including RV cell interaction, structural and functional cellular consequences of the RV infection, and cross-talk between RV and target cells to promote cellular responses. In this respect, I appreciated the new insights into RV infection in polarized cells which were pertinently evoked by U. Desselberger and M.K. Estes in chapter 12.

Alain L. Servin

Glycoprotein Methods and Protocols. The Mucins. Methods in Molecular Biology, Vol. 125; Edited by A.P. Corfield, Humana Press; Totowa, New Jersey, 2000, xvii+506 pp. $ 99.50 (hb). ISBN 0-896-03720-7

This book has 12 major headings and within each there are a series of chapters written by an investigator who has not only used the described methods and techniques but in several cases has also been responsible for their elucidation. The topics covered are: I. Purification of mucins; II. Detection and quantitation of mucin; III. Separation, identification and physical characterization of mucins; IV. Rheology of mucin; V. Mucin peptide analysis; VI. Carbohydrate structural analysis of mucins; VII. Mucin biosynthesis; VIII. Mucin gene detection; IX. Preparation of antimucin antibodies; X. Enzymatic degradation of mucins; XI. Mucin-bacterial interactions; and XII. Cellular and humoral responses to mucins.

Each chapter follows the same general format as the other volumes from this same series. The experts introduce a specific aspect of mucin research and provide a list of materials necessary to address the particular problem. Subsequently, a step-by-step methodological procedure accompanied by the techniques used is presented. Of considerable value are the 'Notes' which accompany each chapter. These comments not only clarify the techniques used but also alert the investigator to pitfalls which may not be readily apparent. While the methods and protocols found in this book have already been published in a variety of scientific journals, this volume brings them all together. There is easy cross-checking of information between chapters since these experts frequently make reference to the other presentations, thereby providing the reader with an appreciation of the strengths and limitations of the methods and protocols which overlap in the different analyses of mucins. This type of appraisal is usually difficult to obtain from research articles specifically for newcomers to this field. In chapter 1 of the volume, for example, a biochemical analysis of mucin which allows one to obtain *reduced subunits* is presented. In chapter 29, which deals with the polyclonal and monoclonal antibody techniques for the detection of mucins, one is made aware of the pitfalls in using monoclonals directed against the epitopes of *reduced subunits* for the detection in native mucins. Therefore, the comments and 'Notes' facilitate the decisions that the investigator needs to make when attempting to deal with mucins.

The major contribution of this book is that the reader has access to the essential biochemical approaches concerning the isolation, identification and quantification of mucins. There can be no doubt that the diversity of the methods presented in this volume offers a considerable service to newcomers to the field and will certainly be a useful reference for laboratories with an interest in glycoproteins. The book may have less appeal for clinicians who may be looking for rapid evaluations of mucins in biological samples from patients. In addition, native mucins are considerably complex and the techniques used to analyze these glycoproteins often require major laboratory instrumentation. This alone may cause some hesitation on the part of investigators to grapple with the mucins in clinical situations. The reader can easily accept after reading this book that an analysis of these complex glycoproteins requires the application of different methods and protocols. Corfield and his associates have provided the scientific community with those basic approaches for the elucidation of the mucin glycoproteins.

This reviewer, however, has noted several quirks in the presentation of this volume.

Unfortunately, in the first chapter on 'Isolation of large gel-forming mucins', there are no references in the chapter to the authors' own published work. However, other chapters cite articles from this laboratory. Thus the reader can find the initial publications concerning the isolation and purification techniques by this research group. There is also a typographical error in reference 17 of this chapter.

There are other typographical errors in the book. One on page 204, another on page 206 as well as on pages 299, 306, and 310. However, there are 506 pages in the book, which indicates that these errors are minimal!

On page 216, in the reference of chapter 17, the title of the article is missing! However, there are 910 references without a fault!

On page 311 (reference 2) and page 321 (references 20 and 21) the citations are PhD theses. However, investigators may have some difficulty in obtaining these manuscripts.

Only one (chapter 16) of the 41 chapters presents a slightly different format than the others. In this chapter the results presented in Figures 5 and 6 are not easy to evaluate and the reader may have to go to the original article in which the data are presented.

As any scientist can realize such quirks in the form of the presentations are insignificant. These mucin experts are to be congratulated for providing the scientific community with a valuable compendium.

Charles Brink

Extracellular Matrix Protocols. Methods in Molecular Biology; Edited by C.H. Streuli and M.E. Grant, Humana Press; Totowa, New Jersey, 2000, xiv+370 pp. $ 89.50 (hb). ISBN 0-896-03624-3

This book is part of a long series devoted to methods in molecular biology; about 30 volumes appear each year. The editors, both from the University of Manchester Wellcome Trust Centre for Cell-Matrix Research, have considerable experience in the field of extracellular matrix. It is becoming well-recognized that the extracellular matrix (ECM) not merely provides a mechanical support to the cells and tissues, but is a major factor in regulating the behavior of the cells by determining which signals from outside reach the cells and by itself signaling instructions for cell proliferation and differentiation and by controlling the movement of cells. Complex and sophisticated new technologies are required to explore the mechanisms of matrix assembly and control of cell function. The editors' purpose is "to present such complicated techniques in a style that is relatively easy to reproduce". Attention is given to the fact that there is already a protocol book for ECM in the IRL Press series edited by Haralson and Hassel in 1995, so this volume is designed to complement and extend rather than repeat the material in that volume.

The volume is divided into four sections dealing with methods that are biochemical, biophysical, molecular biological, and cell biological. There are 29 chapters and each follows the format characteristic of this series: there is first an introduction of 2–4 pages outlining current knowledge of the field and which questions the protocol will answer, next is a list of materials that should be assembled before the methods are tried, then the methods are presented in some detail in the form of numbered steps to be followed. In general, these methods are assembled from information in various papers and brought together in a simplified form that is easy to follow. The most useful feature is probably the final section of 'Notes' that provides numerous hints on handling special tissues, trouble-shooting, alternative paths to follow, etc. – just the sort of practical information that is usually excluded from published scientific reports.

The section on biochemistry contains chapters on how to permeabilize cells to study procollagen assembly (Bulleid), how to quantify collagen crosslinks in tissues (Bailey), expression of laminin (Yurchenko) and collagen in insect cells, and expression of ECM proteins with a strep II tag. Under the heading of biophysics, one finds information on studying fibronectin fragments by heteronuclear NMR, reconstituting integrin in lipid bilayers (Engel), confocal FRAP analysis of molecular interactions (Hardingham), electron cryomicroscopy (Kadler), atomic force microscopy (AFM) measurement of protein–protein interaction strength, and rotary shadowing. The third section on ECM genes includes methods for screening cartilage ECM mutations, preparing tissue-specific knockouts of genes, homologous gene targeting to study ECM assembly (Ramirez), enhancer analysis of collagen genes (Yamada), and gene delivery by retroviruses. While many of these techniques will find limited use because of specialized instruments needs, it is important to note that many of the methods are not limited to the study of ECM. The methods of expression, knockout, gene delivery, etc. can be utilized in the study of proteins not in the ECM. Although the AFM technique is not widely available

at the moment, it has considerable potential for studying all types of macromolecular interactions, a problem that will assume central importance in proteomics.

The final section on cell biology occupies 40% of the volume. The first chapter by Ingber et al. covers interesting micropatterning techniques similar to those used in computer chip photolithography to provide templates for cell growth and ECM deposition. There are chapters on binding of EGFBP and TGF to the ECM, the use of tissue slices for cell culture substrata (Landler), differentiation of neuroepithelial cells and migration of oligodendrocytes. A general chapter on cell adhesion assays (Humphries) is followed by one on tissue engineering using collagen matrices (Kemp) and a more specialized one on tissue engineering of cartilage (Ratcliffe). Solid phase assay of protein–protein interactions is detailed by Mould and the volume concludes with methods for tissue recombinants targeted to basement membranes, fluorescence assays to study cell adhesion, and the analysis of cell–ECM interactions in mammary gland by using knockout mice (Streuli).

The volume is uneven in that not all chapters are of uniform length and not all topics are of equal importance. However, most investigators working in the field of ECM will find one or more methods of interest to them. Even investigators in other fields will be able to find techniques of broad applicability well beyond the scope of ECM studies that could fruitfully be employed in their own studies.

J.F. Woessner

Culture of Animal Cells. A Manual of Basic Technique; Edited by R.I. Freshney, Wiley; Chichester, 2000. xxvi+577 pp. £ 51.95 (hb). ISBN 0-471-1348889-9

Most kinds of plant and animal cells will live, multiply, and even express differentiated properties in a tissue culture dish, provided that appropriate conditions are applied. Such in vitro cell culture systems are technically far more difficult than the culture of bacteria or yeast, however, they have enabled generations of scientists to study cell growth and differentiation, as well as to perform genetic manipulations required to understand gene structure and function. *Culture of Animal Cells* is the fourth edition of a book that has been extremely useful both as a practical laboratory manual and as a textbook for beginners. In 28 chapters and more than 570 pages the book covers most relevant areas and provides many useful protocols.

The book begins with a general introduction about tissue culture, its advantages and disadvantages. It is followed by a chapter describing the biology of cultured cells and more generally the evolution and origin of cell lines. The following chapters (3 and 4) contain a wonderfully clear description of layout and all basic equipment for a tissue culture laboratory unit. They are followed by a basic course on sterility (chapter 5) and laboratory safety (chapter 6). The book then continues with five chapters on everything you will need for culturing cells or tissues: culture vessels, media preparation and sterilization. Chapters 11 and 12 introduce primary cultures and cell lines, respectively. The next two chapters are devoted to cloning/selection and to cell separation techniques. Next cytological characterization (chapter 15), differentiation (chapter 16), and transformation (chapter 17) are discussed. In the following the reader learns how to cope with contamination. Cryopreservation (chapter 19), cell counting (chapter 20), and cytotoxicity testing (chapter 21) precede the very important chapter 22 on specialized cells. Here and in the following chapters on tumor cells (chapter 23) and organotypic cultures (chapter 24) many useful protocols and practical tips can be found. Chapter 25 talks about scaling up cultures and chapters 26 and 27 contain specialized cellular and molecular techniques. Finally the book ends with a very useful chapter devoted to problem solving. In addition a trade index, glossary, and extensive references are supplied. The book is well indexed and the supplier index even contains Internet addresses.

To whom would this kind of book be useful and what could be improved? The book is clearly structured, very detailed and contains necessary background information for less experienced users and serves as a rich source of useful protocols. However, it is more a textbook than a handy laboratory manual or quick reference. It takes some time to find the protocols within the text and I could imagine offering in future editions of this classic all cell culture protocols at hand as an indexed paperback version. I also think that a chapter on stem cells has to be included. Some techniques such as cell migration assays, measurement of transepithelial electrical resistance and metabolic labeling are briefly mentioned but would deserve more detailed explanations. In addition assay techniques for apoptosis and three-dimensional collagen cultures should be included in the next edition. The pictures of laboratory equipment are a bit outdated and would benefit from a face lifting. However, I like the book and I am confident that all researchers working with tissue culture systems will find this book a great source of frequent consultations.

Lukas Huber

Principles and Techniques of Practical Biochemistry; Edited by K. Wilson and J. Walker, Cambridge University Press; Cambridge, 2000, xviii+784 pp. £ 27.95 (pb). ISBN 0-521-65873-X

It is becoming increasingly recognized (but, alas, much more slowly by most students) that modern biochemistry is an interdisciplinary science with which cell biology, microbiology, and genetics (to name only a few disciplines) have become extensively integrated. The principles and techniques of molecular biology have been primary and pervasive catalysts of this development. Indeed they have been responsible for much of the remarkable growth of the molecular biosciences in the past three decades. It is not surprising therefore that a variety of laboratory techniques (and many of their variants) that were essentially characteristic of each of these biosciences are nowadays frequently brought together in the investigation and elucidation of biological problems. However, fruitful application of these techniques requires not only technical dexterity but also a good understanding of their underlying principles (which are very frequently based in physics, chemistry, and mathematics) and statistical treatment of the results of experiments. This largely explains why the majority of undergraduates majoring, or involved in research, in biochemistry experience difficulty in integrating so many areas of knowledge that are still largely taught in isolation one of the other. This compendious but accessible book should prove to be a reliable, useful, and appreciated source of understanding and assistance on a broad range of laboratory techniques for such students.

Now in its fifth edition, this book first appeared a quarter of a century ago. Because several new authors have contributed new chapters or revised those in the preceding edition, there is much that is new in it. Retained has been the original broad aim of the editors, that is "to concentrate on those techniques and principles which underlie practical exercises that undergraduates in all biological sciences can expect to encounter in their practical classes and to cover in less detail the more sophisticated techniques that have made possible the advances they will learn about in their lectures and associated reading" (p. xiii). Five of the authors (including the editors) are at the University of Hertfordshire, one each at the Metropolitan University of Manchester, Oxford Brookes University and the University of Central Lancashire, and two are at the National Institute for Biological Standards and Control, all in the UK.

The 15 chapters range in length between 29 and 79 pages. They fall broadly into two groups. Those that focus on techniques for study of

a particular category of biomolecules (i.e. 1, which deals mainly with bioenergetics and metabolism; 2 and 3, with nucleic acids; 6, with proteins; 7, with enzymes; and 8, with cell surface receptors and transporters) constitute the first group. In these, theoretical aspects of the particular biomolecules are neatly integrated with the variety of methods available for their investigation. The second group consists of chapters that deal with particular physical techniques (i.e. centrifugation, various types of spectroscopy, spectrometry, electrophoresis, chromatography, radioisotopes, and electrochemistry) and with immunochemical techniques. As is only proper because of the dominating role the techniques of molecular biology play in current research, two chapters (126 pages in total) are dedicated to them. They include: enzymatic manipulation, restriction mapping, isolation and separation of nucleic acids; nucleotide sequencing; the polymerase chain reaction; construction and screening of gene libraries; cloning vectors and foreign gene expression; and whole genome analysis. Practical hints, the results of much experience, enrich most sections. Although a good amount of prior knowledge is expected, there is little here that should be beyond the capability of majors in biochemistry and other molecular biosciences in the latter part of their program to meet.

Uniformity of style is an attribute of all chapters, with key words or phrases being highlighted in color and also presented in alphabetical order at chapter end. Examples of well selected calculations (with answers) are provided in most chapters. Suggestions for further reading (mostly to books published within the past decade) conclude each chapter. I found very few typographical errors, the most significant being in the value for the atomic mass unit (Da). With some 2000 entries the index is very comprehensive.

I was very impressed with this bulky book. A copy should be available in every bioscience department and research library. That those students planning a research career in a molecular bioscience will find it a valuable and trustworthy companion during their studies I have little doubt.

F. Vella

Hepatocellular Carcinoma. Methods and Protocols. Methods in Molecular Medicine; Edited by N.A. Habib, Humana Press; Totowa, New Jersey, 2000, xiii+302 pp. $ 99.50 (hb). ISBN 0-896-03785-1

Throughout the world hepatocellular carcinoma (HCC) is the sixth most common cancer and the third most common cause of death from cancer. Liver cancer incidence is increasing, especially in the developed countries, and is almost always fatal. The 5-year survival rate in the USA is only 6% and this level is still lower in developing countries. Early diagnosis and liver transplantation are, at present, the most effective treatments but, as known, transplantation is not easily applicable because of the donor limitations. The relationship between HCC and previous infections with hepatitis viruses and exposure to aflatoxin B1 is well documented although the genetic basis of hepatocarcinogenesis is still poorly understood. It is therefore of the utmost importance to better understand the pathogenesis of HCC and to make all efforts for preventing viral hepatitis and its progression to cirrhosis and to study new strategies for its therapy. At the moment, this type of study is still limited and it is therefore quite relevant to underline the positive efforts for trying to have an up-to-date view of the clinical and scientific knowledge in the field of hepatocarcinogenesis.

Hepatocellular Carcinoma: Methods and Protocols, edited by Nagy A. Habib, is mainly a manual focusing on the methods applied in clinical and research laboratories but it is also a valuable scientific review for those interested in understanding the clinical management of patients with HCC. The book is a useful and detailed overview of most, if not all, of what is presently known on the etiological factors, molecular and biological markers characteristic of HCC and concludes with the approaches for innovative therapy strategies.

The editor has enlisted 49 authors for 20 chapters with the first two focused on the general description of the clinical problem and the treatment modalities of the patients. The following chapters, 3–5, describe the main etiological factors involved in HCC while chapters 6–11 deal with the molecular changes associated with HCC and identify possible targets for therapy. Finally, chapters 12–19 analyze the use of various vector systems for possible gene therapy approaches. Chapter 20, at the end, describes the first protocol, to be approved, for p53 gene therapy of liver tumors. All chapters are mainly focused on laboratory methods and protocols and they are generally characterized by a brief description, at times repetitive, outlining the problem and introducing the protocols utilized in the specific chapter. The protocols are generally well detailed and include many hints for the successful execution of the methodology. These protocols often cover general approaches for the study of cancer and therefore their usefulness is not only limited to scientists and/or clinicians working with HCC but it may be extended to technicians, scientists and clinicians working with tumor cells, cancer biopsies, and clinical and diagnostic management of tumor patients. Chapter 20 may be particularly helpful for clinical researchers involved in the practical planning of protocols for human gene therapy trials. The description of the first trial, to be approved by the gene therapy advisory committee, for the application of a clinical protocol, involving the replacement of a p53 functional gene in liver tumors, may find useful applications for other types of tumors.

Concerning the general structure of the book, an introductory chapter with an overview of the possible different biological, genetic and environmental agents known to be important factors predisposing to HCC would have been useful, especially for those who are not actively involved in HCC research. Information on these general and biological aspects can be found dispersed in the different chapters. In particular, these problems are briefly outlined in the first chapter (whose main purpose, however, is on the clinical aspects of HCC). The clear, detailed and exhaustive description done by the authors of the clinical problem would get, in my opinion, great profit from a more detailed biological introduction. Some of these biological analyses can be found in the introduction of chapter 6, dealing with the impact of hepatitis B and C viruses on HCC. In this chapter, the efforts for trying to characterize the biological pathways leading to HCC in order to find strategies for identifying specific targets for therapy trials are evident.

This criticism, however, should not diminish the usefulness of this book, which clearly declares to be mainly a collection of methods and protocols utilized in the characterization and management of HCC, rather than a theoretical book on the molecular problems involved in hepatocarcinogenesis. A cultural and scientific message, however, clearly emerges: it is evident that much more has to be done and known for a successful treatment of HCC. This implies that many more scientists should be involved and more research should be financed in this field, in order to better identify the possible targets for successful therapeutic approaches. The frustration of the clinicians is clearly manifested in the conclusions of the first chapter written by Usastoff and Habib. Following an overview of the numerous therapeutical strategies they conclude with the old adage "whenever there is a long list of treatment options, it is likely that none of them is perfect". This demands future research and innovative treatments for possible solutions for this devastating tumor. The increased incidence of this tumor in the developed countries might hopefully stimulate the scientific community to consider this tumor a primary health problem deserving priority in which it is important to invest: people, time, and money. Independently of the infective and environmental factors, for which prevention should be promoted, HCC should be considered, first of all, a biological problem, whose understanding should lead to effective and efficient therapies. That we are still far from this objective is clearly evident from this book, which should be a useful starting source of reference for students and investigators who would like to enter this stimulating research field, open to new ideas and contributions. New ideas and strategies might contribute to prolonging the life expectancy of HCC patients.

Sergio Barlati

Medical Cytogenetics; Edited by H.F.L. Mark, Marcel Dekker; New York, 2000, xvii+680 pp. $ 195.00 (hb). ISBN 0-896-03694-4

Hon Fong L. Mark has written a book on medical cytogenetics out of an apparent need for a book providing an overview of this field. The book is aimed at "physicians, and scientists in training or in practice, medical and advanced undergraduate students interested in medical genetics, cytogeneticists studying for the certifying examination in clinical cytogenetics offered every three years by the American Board of Medical Geneticists, and board certified geneticists desiring a review of the field of cytogenetics for recertification and other purposes". It appears that the book contains elements from two sources, some chapters have been contributed by well known experts upon invitation, whereas other chapters have been written by the author, alone or together with co-workers.

Writing a textbook is no minor undertaking, and we all want good textbooks on interesting topics. Medical cytogenetics is a topic worth a textbook, and the author's efforts are certainly worth appreciation. However, the overall impression is not that of a book which is significantly better than other relevant textbooks. Furthermore, for an expert who knows the world both inside and outside the USA, the book seems more American than truly international. *Medical Cytogenetics* does contain good chapters, and there is no doubt that virtually anyone within the rather broad envisioned audience will find something of interest in the book. On the other hand, I suspect that very few readers will find an interest in the book from one end to another. *Medical Cytogenetics* thus seems more valuable as a handbook than as a textbook. There are probably two mechanisms behind this result. First of all, while targeting a broad and mixed audience is likely to be good for the sale of the book, it also means that for the book to reach its full audience, any part of the book can only reach part of that audience. Secondly, the mixture of writers have contributed chapters of somewhat uneven level and quality. Some chapters are therefore most relevant for readers with little or no prior knowledge, whereas other chapters are more accessible to readers who have a certain level of prior knowledge.

As far as the individual chapters are concerned, the chapters on myeloid cancers, solid tumors, and chromosome instability and fragile sites stand out as very good indeed (chapters 11, 13, and 14). The chapter on human cytogenetic nomenclature makes the best out of a not very exciting topic, and is worth reading for someone needing to learn the rules of human cytogenetic nomenclature. At the other end of the scale, chapters 12 (cytogenetics of lymphoid neoplasms), 16 (cytogenetics in transfusion medicine), and 17 (applications of FISH) are not impressive, and chapter 18 (molecular cytogenetics technologies) is professionally rather unfortunate. It comes from a high-quality laboratory, which has developed one of two competing techniques for multicolor karyotyping of human chromosomes. Consequently, only one of the two techniques (spectral karyotyping, SKY) is dealt with, and the reader is left with the false impression that the other, and more widely used, technique (multicolor FISH, M-FISH) is both newer than, and inferior to, SKY. I'm well aware of the commercial interests involved, and I have witnessed the bitter rivalry at conferences, but this shouldn't be carried on into a book aiming at providing the reader with unbiased information on medical cytogenetics.

The remaining chapters fall between these extremes, and would for most parts be of primary interest as a first introduction to the topics dealt with, as they seem to be at a more basic level than the chapters contributed by the experts. This impression is further enhanced by a few factual errors. It is thus claimed for instance that SKY is based on color ratios (it is truly based on color combinations) and that PRINS is derived from in situ PCR (PRINS is an older technique than in situ PCR, so that can hardly be the case). At the same time the PRINS technique is also incorrectly referenced. The presence of these errors falls well in line with the problems relating to chapter 17, and the (presumably unrecognized) American nature of the book to form the impression outlined at the beginning of this review.

Jørn Koch

Affinity Chromatography. Methods and Protocols. Methods in Molecular Biology; Edited by P. Bailon et al., Humana Press; Totowa, New Jersey, 2000, x+230 pp. $ 79.50 (hb). ISBN 0-896-03694-4

This book is an important addition to the Methods in Molecular Biology series. It pulls together many affinity chromatography techniques in one book that can be used both by beginners and by experts. The book is divided into 19 chapters representing the work of 36 contributing authors. Each chapter addresses a specific affinity chromatography method. The chapters are organized with an introduction, followed by a list of reagents, methods, examples of use of these methods, and finally notes elaborating on details or problems related to the methods. At the end of each chapter is an excellent and useful list of references. For the most this format works well, but several times one finds oneself wishing that each example had been written up separately so that one does not have to flip forward through several pages to find out what buffer B is and then flip backwards to the Notes to find out the details of why one is using buffer B instead of A, etc.

Chapter 1 is an overview starting with the introduction of affinity chromatography in a 1968 paper by Cuatrecasas, to its widespread use today (in more than 60% of all purification protocols), to its evolution into high throughput analytical methods for protein–protein interactions (BIAcore surface plasmon resonance).

Chapters 2–10 deal with immunoaffinity chromatography, which is probably the most widely used application of affinity purification. In chapter 2, the authors discuss weak affinity chromatography, which they define as involving ligands with a $K_a < 10^5 M^{-1}$. They show mathematically how weak affinity can be overcome by using a high amount of ligand, and how this can sometimes increase the chromatographic resolution and pick up interactions that would be missed by only using ligands (in this case monoclonal antibodies) with a high affinity ($> 10^5$ M^{-1}). Protocols are then given for immunizing mice, selecting hybridomas, purifying monoclonals, packing HPLC columns, etc., all complex procedures that can be readily carried out by someone experienced in the field but are definitely not for the beginner. Chapter 3 deals with fluidized bed receptor affinity chromatography, in which the support beads float freely rather than being packed in a column making it possible to load particulate-containing samples which would clog chromatographic columns. For example, disrupted cell cultures can be loaded without removing cells or cell debris. There are also two examples of refolding proteins from inclusion bodies and loading the refolded proteins together with the precipitated proteins onto a fluidized bed. The technique worked well for the proteins studied but there should be a caveat that protein refolding is not often as simple and straightforward as these examples suggest.

Chapter 4 gives very useful methods of optimizing the coupling of antibodies to protein G Sepharose using dimethylpimelimidate to orient the antibody for maximum antigen binding. Chapter 5 discusses methods for purifying different subtypes of monoclonals, starting with a standard protein A method and going on to thiophilic and immobilized metal ion affinity chromatography for cases in which protein A is not suitable. Chapter 6 presents a very interesting alternative to protein A for antibody purification, a peptide mimetic (PAM) designated TG19318. When immobilized, this support can be used to purify IgG from a broad spectrum of species, but more important, it can be used to purify IgM, IgA, IgE, and IgY, all of which are difficult to purify by other means. The PAM support is also resistant to harsh sanitizing reagents and leaching. Chapter 7 addresses the conditions for periodate oxidation of antibodies for immobilization on hydrazide-activated supports, and chapter 8 discusses the synthesis of peptides corresponding to the hypervariable segments of monoclonal antibodies (the authors state that in most cases these peptides will not bind the antigen after immobilization). In chapter 9, the authors put forth a simplified method to deplete serum of antibodies (i.e. carrier

antibodies) by using ground-up nitrocellulose (NC) membranes, which spontaneously bind any protein, to immobilize the carrier antigen. This antigen-containing NC is then incubated with serum containing carrier antibodies as well as the antibody of interest. It is not clear how to ensure that all the NC binding sites are saturated with the carrier antigen in order to prevent the loss of the desired antibody due to non-specific binding to the nitrocellulose.

The last chapter in this group, chapter 10, is called Immunoaffinity chromatography and describes two ways of immobilizing antibodies through primary amines, and some elution conditions. It is at this point that one wishes that the presentation of immunoaffinity methods had been better organized, with all the immobilization methods and their pros and cons listed together, followed by binding and then elution options. Much of this material is repeated from chapter to chapter.

Chapter 11 on affinity partitioning of proteins gives some rather complex methods for extracting proteins into one phase or another using a ligand that is bound to one of the polymers used for extraction. It is not made clear under which circumstances one would use this technique over other more conventional affinity ones. Chapter 12 describes boronate affinity chromatography using several commercially available supports. The boronate will specifically bind to *cis*-diol-containing compounds and is therefore a useful tool for purifying glycoproteins and separating RNA from DNA. Boronic acid derivatives also bind to many serine proteases and can be used in their purification. Also, ligands such as NAD^+ or ATP can be bound to the boronate resin and these immobilized molecules can then be used for affinity purification of many enzymes. The next chapter on dye ligand affinity chromatography concentrates on purifying and immobilizing the dyes (many of which are commercially available already immobilized) rather than on the applications of dye chromatography, but it does go into some basic screening and purification protocols. The chapter on DNA affinity chromatography describes in considerable detail the synthesis and immobilization of oligonucleotides. Several references are given on the use of these supports in the purification of DNA binding proteins, etc.

Chapter 15 gives a novel approach to the important problem of removing bacterial endotoxin from protein solutions by using immobilized histidine to bind it. It gives an immobilization protocol but does not mention whether the commercially available support (from Sigma Chemical Co.) works as well. Binding conditions and protein recoveries are presented for several different proteins at different concentrations and pHs. Chapter 16 discusses the use of Western cross blots to check for cross-reactivity of antibodies. This is a technically cumbersome procedure whereby antibodies reacting with one set of antigens on a blot are electrophoretically transferred to another blot. Because of the technical limitations, only positive results are meaningful, since a negative result could well arise from a failure in the technique. Chapter 17 on affinity perfusion chromatography gives probably the clearest and most organized presentation of methods for immobilizing antibodies on a rigid support using four different chemistries. These are the same as used in earlier chapters of this book except that POROS resins are used. These resins are large-pore large beads that are very rigid and allow for very rapid flow rates, high ligand densities, and high binding capacity. The use of POROS resins discussed in this chapter is mostly for high-throughput rapid analysis. The methods can be scaled up, however, provided that the cost of the resins is not a concern.

The final two chapters deal with Phage display: affinity selection by biopanning and identification of peptides as model ligands. This is relatively new, important, emerging technology for identifying affinity ligands. It might have been better to include these chapters in a different volume as they do not pertain to chromatography as such. There are protocols for biotinylation, insect cell infection, mammalian transfections, phage titering and DNA isolation. The authors assume the reader is familiar with bioinformatics and GCG software. These are pretty straightforward procedures for many molecular biologists but probably not for the readers who would be most likely to use this book, i.e. those engaged in protein purification and biochemical research.

Despite some of the drawbacks mentioned above, this book would be a useful addition to the resources of anyone involved in protein purification. For the most part, the protocols are easy to follow and the references cited at the end of each chapter are very useful to obtain further information. Perhaps in the next volume of this series the authors could discuss the many affinity chromatography tags that are expressed as fusions with recombinant proteins to aid in their purification, e.g. GST, MBP, 6His, and many others.

Ruth Lehr

Booklist No. 157

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