

Book Reviews

The Liver Biology and Pathobiology; Edited by I.M. Arias, (ed. in chief), J.L. Boyer, N. Fausto, W.B. Jakoby, D. Schachter and D.A. Shafritz, (ass oc. Eds.); Third Edition, Raven Press; New York, 1994; 1,622 pp. \$305.00. ISBN 0-7817-0133-3

With a new edition every sixth year 'this book strives to bridge the widening gap between the amazing advances in basal biology and their application to liver structure, function and disease'. It expands with its subject, now with 7 sections, 84 chapters, and 168 contributing authors.

The sections comprise an introduction, where V.J. Desmet gives a thoughtful overview of the status and problems of organizational principles, followed by 'The Cells', 900 pages, with 19 chapters on hepatocyte organization, including organelle functions, regulation of gene expression, nuclear entry, and endocytosis, 15 chapters on hepatocyte metabolism, from energy metabolism to detoxication and vitamin and metal metabolism, 6 chapters on bile secretion, 2 on sinusoidal cells, and 3 on the extracellular matrix. The section 'Interrelated Cell Functions' in 11 chapters presents signal transduction, the roles of G protein, inositol triphosphate, calcium, insulin, cytokines, eicosanoids, nitrous oxide and growth factors, and the section 'The Organ' discusses structure-flow relations in 3 chapters.

In 'Relation of the Liver to Other Organs' the influence of liver function on other tissues as muscle, fat, brain, bone, blood and the endocrine and immune systems is analyzed in 8 chapters, and this aspect is expanded in 10 chapters in the section 'Pathobiologic Analysis of Disease Mechanism' to cholestasis, portal hypertension, liver fibrosis, infection with hepatitis virus, and cellular injury from ethanol, immune mechanisms, and neoplasia inducing chemicals.

The concluding section 'Horizons' selects – as in previous editions – areas with remarkable advances expected to have great impact on hepatology in the future. Chapters from this section in preceding editions have been included as chapters in other sections of following editions, confirming the expectations of the editors. In the present edition 7 chapters may be viewed as an analysis of basic problems needed to be resolved to modulate liver function, i.e. to find more specific and less invasive alternatives to liver transplantation. It comprises identification of the hepatocyte stem cell, transplantation of hepatocytes, targeting of nucleic acids to nuclei, understanding of cell cycle regulation and apoptosis, immunomodulation, and designing genes for transgenic models.

Clearly the section 'The Cell' is pivotal, as to volume as well as conceptually, with emphasis on progress in molecular and cellular biology.

These disciplines may dominate the exploration of most or all aspects of human biology and pathobiology, but they have been particularly productive to promote understanding how the liver succeeds to perform the multiple tasks required to keep the rest of the organism in good shape, and what goes wrong in liver disease. The section described how the cell receives and transduces signals, how they affect transcription of the large number of genes the liver can express (accounting for more than 5000 'liver functions'), the effect of nuclear export, RNA processing with translational control of initiation and prolongation,

and protein folding and export or degradation. Part of the knowledge presented is derived from the study of cells other than the hepatocyte, but in spite of that of evident relevance for the liver. In the chapters on metabolism classical biochemistry and physiology maintain their role as key disciplines, but with developments largely supported by molecular biology.

Perhaps the most intriguing questions in hepatology, biologically as well as clinically, is how the liver exerts an influence on other organs. As stated in the introduction to that section 'the liver is a window through which one may view much of the functions of the body'. Unfortunately the view through the window still is rather blurred, although progress is reported. This is true also as to the pathobiological mechanisms underlying cholestasis and other processes of clinical interest, discussed on the background of basic science as a valuable supplement to standard textbooks.

Evidently the editors' intention is to carry the reader through increasing levels of organization. Fortunately they do not adhere dogmatically to this plan, but have allowed each author to present findings and interpretations within their own field of expertise. In return they have written stimulating and inspiring articles about their favourite subjects. Thus results in some overlapping and occasionally in differences in points of view. However, repetitions do not exceed what may be required to read each chapter as an entity, and differences of opinion are natural dealing with subjects close to the limit of present knowledge. It also follows from this supposed editorial policy that chapters are heterogeneous, both in volume and style. Some authors carefully provide the reader with background knowledge, others go more directly to the subject.

The lay-out of the book is of the highest standard, with good introductions, summaries and tables and figures. It is recommended to clinical hepatologists for whom it may be difficult to keep up with the expanding original literature and will 'find in this volume glimpses into the current state and future direction of our discipline and perspectives that lead to better understanding of liver function and disease', but it will enrich any reader prepared to make the effort. It should be obligatory reading for anybody who intends to engage in liver research. Presented by this extensive amount of facts about the liver it may be frustrating – or stimulating, depending on the state of mind – to realize how much needs to be learned before we understand what the liver can accomplish, how and why. The statement of K.S. Zaret "Prospects are bright that in the future we will ameliorate liver dysfunction by intervening in the genetic regulatory pathways that control hepatocyte differentiation" is undoubtedly true, but there is a long way to go. Future editions of this book will, like the present one, help to show the way.

Niels Tygstrup

Cellular Cancer Markers; Edited by C.T. Garrett and S. Sell; The Humana Press; Totowa, 1995; xi + 484 pp. \$ 125.00. ISBN 0-896-03210-8

Tumor or cancer markers can simply be defined as molecules which indicate the presence of a malignancy. The application of these molecules to cancer diagnosis and management is presently one of the

biggest growth areas in laboratory medicine. Traditional tumor markers (e.g. CEA, AFP, and PSA) are assayed in body fluid such as serum. The aim of this book is to give an update on cellular cancer

Information about books for review in FEBS Letters should be sent to: Professor J.E. Celis, Department of Medical Biochemistry, Ole Worms Allé, Building 170, University Park, Aarhus University, DK-8000 Aarhus, Denmark.

markers. These cellular markers are defined in the Preface as molecules which are "not released into serum or other body fluids in any appreciable quantity". The main emphasis is on c-oncogenes and suppressor genes although differentiation antigens and markers of chemotherapy resistance are also discussed. Following a comprehensive Introductory Chapter, selected c-oncogenes and suppressor genes such as *ras*, *c-myc* and *p53* are discussed in Chapters 2, 3 and 4. Each of these Chapters focus on basic mechanisms of gene activation as well as on potential clinical applications. As regards possible clinical uses, most of the emphasis is on disease prognosis rather than diagnosis. Surprisingly, no Chapter was devoted to the *c-erbB-2* gene which is perhaps one of the most widely investigated c-oncogenes from a clinical point of view. Chapters 5–9 discuss molecular alterations in a number of different malignancies such as gynaecological, colorectal, breast and lung cancers as well as melanomas, Hodgkin's and Non-Hodgkin's lymphoma. One common malignancy which is omitted is prostate cancer. These Chapters are of variable quality, especially in the

inclusion of up-to-date references. Thus, the Chapter on Non-Hodgkin's lymphoma contained references only up to 1992 while the Chapter on breast cancer included publications up to the end of 1994. Chapters 14, 15 and 16 concentrates primarily on the exploitation of the molecular alterations in malignancy for therapy. Thus Chapter 14 discusses P-glycoprotein but not other markers of chemotherapy resistance while Chapters 15 and 16 describe the use of genetically engineered monoclonal antibodies and antisense oligonucleotides.

In summary, this is a good introduction to what the authors call "cellular cancer markers". The publication is timely and will be of value to cancer researchers, clinical chemists/biochemists and commercial companies interested in exploiting recent advances in molecular carcinogenesis for the development of new diagnostic and management tests. One hopes that in the future, this book will be expanded, updated and revised as molecular markers find increasing clinical applications.

M.J. Duffy

Advances in Second Messenger and Phosphoprotein Research. Molecular and Cellular Mechanisms of Neurotransmitter Release; Edited by L. Stjärne, P. Greengard, S.E. Grillner, T.G.M. Hökfelt and D.R. Ottoson; Raven Press; New York, 1994; xxii + 569 pp. \$ 157.00. ISBN 0-7817-0220-8

This volume in the series Adv. Sec. Mess. and Phosphoprotein Res. represents the Proceedings from a Wenner-Gren International Symposium on the topic which is the title of the book. It summarizes the recent developments in the understanding of the intricate molecular mechanisms underlying transmitter release. It contains focused reviews on synaptic vesicle proteins, pathways for transmitter release, Ca^{2+} channels and their role in vesicular release and finally an analysis of mechanisms for quantal release both in the central and peripheral nervous systems. The outline of the proteins in the vesicular and plasma membrane of the synaptic complex of docked vesicles is very useful and the discussions of the spatio-temporal relationships between vesicular release and changes in the intracellular Ca^{2+} concentration are the results of front line research. In this context the chapters on Ca^{2+} signalling

and Ca^{2+} channels are highly appropriate. The chapters on mechanisms governing glutamate release from isolated nerve endings or more intact nerve cell preparations provide up-to-date information about its regulation. Discussions of quantal release are useful and the notion of quantal variance receives pertinent attention.

Overall the Editors of the Volume are to be congratulated for the excellent coverage of this rapidly moving area of neuroscience. The multidisciplinary approach by having contributions from neurochemists as well as neurophysiologists has been a success. This book is very useful for everyone working in this area of research. In this regard, the subject index is useful.

Arne Schousboe

Micelles, Monolayers, and Biomembranes; Edited by M.N. Jones and D. Chapman; Wiley-Liss; New York, 1994; xii + 252 pp. \$ 36.95. ISBN 0-471-56139-8

This book covers a broad spectrum of topics on the structure and organization of living matter that are dependent on hydrophobic interactions. In the first chapter the 'actors' involved in the hydrophobic effect (detergents, membrane lipids, and proteins) are introduced. This is followed by a detailed consideration of the use of the lipid monolayer system as an experimental model of biological membranes. Of particular interest is the current use of fluorescent dyes with which to visualize microheterogeneity (arising from limited free mixing of lipids), analysis of area-pressure curves, and the use of the system to study protein adsorption. In a similar way, chapter 3 introduces us to fundamental aspects of detergents. The chapter is centered on bile salts and SDS, whereas non-ionic detergents, which are important for solubilization of membrane proteins in functional form, receives little attention. In the following chapters a wide variety of subjects is reviewed, among which can be mentioned: the various lipid phases, liposomes and the problems attending their use for targeting of substances into cells, detergent solubilization of biological membranes, the role of lipids for membrane protein function, the fluidic-mosaic model of membrane structure, membrane reconstitution, the effect of hydrophobicity in anchoring of signal peptides, membrane dynamics (rotational and lateral diffusion). These chapters contain many interesting illustrative examples, but nevertheless I have to confess that during the reading I felt somewhat unsatisfied. To a large extent, this has to do with what I perceive as a weakness in the overall planning or design of the book. The purely physico-chemical parts are not always

well coordinated with their application on biological systems. In the foreword the authors point out that a full treatment of the subject of hydrophobicity would require several book volumes. Alternatively, I propose that this situation would have called for stricter planning. Indeed, the task would have been easier, if the authors had restricted themselves to micelles and membranes, in accordance with the title of the book. Instead they have focused too much on favorite topics, without giving enough consideration how these really fit into a coherent treatment of the subject, based on a set of unifying themes. For instance, there are interesting data on the role of hydrophobicity for assembly of tubulin and β -casein micelles, but the generality of hydrophobicity for association of e.g. membrane proteins is not discussed. In their treatment of the hydrophobic properties of proteins, the authors insist on taking a broad view, with the result, I fear, that the fundamental differences between watersoluble and integral membrane proteins do not clearly emerge. In some places (e.g. detergent solubilization and models of membranes) the treatment is perhaps also too traditional. The strongest parts of the book are those dealing with lipids and the authoritative treatment of the physical chemistry of detergents and lipids. Despite any shortcomings it is, in this area of cellular and structural biology, to be welcomed as an introductory text on the biological significance and physico-chemical basis of hydrophobicity.

Jesper V. Møller.