

Hitting the Mark

Drug Targeting. Organ-Specific Strategies. Edited by *Grietje Molema* and *Dirk K. F. Meijer*. (Series: Methods and Principles in Medicinal Chemistry, Vol 12. Series editors R. Mannhold, H. Kubinyi and H. Timmerman.) Wiley-VCH, Weinheim 2001. 381 pp., hardcover € 139.00.—ISBN 3-527-29989-0

The continuing search for improved treatments for debilitating and life-threatening diseases commonly follows one of three avenues: screening natural products to identify novel drugs, using medicinal chemistry to create improved drugs, or developing a targeting strategy (prodrugs and drug carriers) with the aim of increasing disease-specific drug targeting whilst minimizing normal tissue exposure. The modern concept of drug targeting was born out of the pioneering work of Paul Ehrlich. In the early 1900s Ehrlich imagined effective chemotherapy as a “magic bullet” speedily localizing in the offending target cells. The renaissance of interest in drug targeting during the last 30 years has led to an explosion in basic research and the transfer of drug-targeting strategies into routine clinical practice.

Apart from published collections of research papers, and books focused on a single aspect of targeting, there have been few books that set out to give an overview of the state of the art in the field. This excellent text fills that gap and it is a “must” for the bookshelves of academic and industrial research scientists active in the field. The clear pre-

sentational style (including many diagrams and summary tables) provides an excellent reference source for newcomers and graduate students alike. The basic concepts of drug targeting at both the cellular and subcellular levels are clearly introduced, and drug-targeting technologies are described with emphasis on recent clinical progress. Many challenges remain if the principles of drug targeting are to be widely applied outside cancer chemotherapy. These challenges are discussed eloquently with clear insight into the past development and current status of the field.

Some minor criticisms. Many chapters focus on specific topics, such as tumor targeting, pulmonary delivery, and colon targeting. Many readers will find these chapters comprehensive and informative. However, certain chapters are rather narrow as the authors have focused on their own research specialization—a limitation common to all such multi-author books. This inevitably leaves some gaps. There is little mention of passive tumor targeting based on the enhanced permeability and retention (EPR) effect, or passive targeting usually referred to as nonspecific macrophage capture. Antibody-mediated targeting and protein constructs for targeting, both of which have been slow to realize clinical benefits, are discussed at greater length than liposomes and polymer conjugates. Although the latter often rely on the less intellectually seductive idea of passive targeting as a means to improve therapeutic index, they have generated many more products in routine clinical use. Organizationally the book is sometimes disjointed. For example, the chapters describing tumor vasculature targeting and vasculature targeting in inflammatory disease might have been placed in series. It would have been advantageous to include the titles of papers in the bibliography. These are minor irritations. The book is excellent and well researched.

Besides the scientific critique, the chapters describing tools and techniques are particularly helpful. They include phage display technology, recombinant approaches for the generation of protein constructs, use of tissue slices in drug-targeting research, and pharmacokinetic and pharmacodynamic modeling. A welcome addition to the library!

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The Biochemistry of Cell Signalling. By *Ernst J. M. Helmreich*. Oxford University Press, Oxford 2001, 328 pp., softcover £ 29.95—ISBN 0-19-850820-4

Cellular signal transduction is a young branch of biochemistry which has rapidly grown in importance in the last ten years. It has become established in the university teaching programs in the area of biochemistry and biology, and as such this textbook written by Ernst J. M. Helmreich is a welcome aid.

The author does not claim to describe all the earlier investigations or imaginable dodges of signal transductions, rather he conveys the biochemical concepts that can be observed in the generation of the signals and their regulation. This is also reflected in regards to the content and the formal layout of the book. One signal pathway is not stoically worked through after another, instead the arrangement is oriented from a mechanistic and functional point of view. The first part, which covers about half of the book, presents in eight chapters the so-called machinery of cellular signals, and elucidates this using the most important examples. In the course of this, details and also many special cases are mentioned. In the three chapters each of the

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second and third part, the implementation of the principles of the regulation of gene expression and the control of the cell cycle, apoptosis, and the immune response are clarified. Finally the fourth part shows how error functions in signal transduction can lead to the development of cancer. With a deliberate abandonment of a large number of factors, the author, however, has also left out some important branches such as, for example, signal transfer in neural systems. One would search in vain in this book for channels and neural receptors. Possibly he sees these themes as being handled in sufficient detail in standard biochemistry textbooks. Praise should be given for the 9-page index of abbreviations at the start and the 20-page glossary at the end of the book, which helps not only the beginner to get on board.

The signal pathways described are illustrated by numerous schemes, the graphical resolution of which is sometimes only just satisfactory. In addition it must be said that many symbols and arrows in these pictures are not understandable for beginners without further details, and that they sometimes appear to be noncommittal. For that the author is not necessarily to blame, as the current status of research has numerous gaps and inconsistencies. Perhaps a more uniform design of the illustrations would have been better. In addition, many schemes appear to be very static so that the development of the process can not be easily envisaged. There is a large number of three-dimensional protein structures in which ribbon representations are shown, but unfortunately none are in stereoview. Besides the pictures in grayscale throughout the text there are 30 high-quality color plates in the middle of the book, although some of them appear rather small. There don't seem to be any printing errors, while one or more (excusable) lapses in content can be found. For example, Ras is not linked to the regulatory subunit of PI(3) kinase and Mx proteins are not GAPs for other GTPases.

The separate chapters each treat a particular aspect of signal transduction and are self-contained. At the same time, the author—with the long-standing routine as a lecturer—is successful in writing the entire book as a unified entity. He uses the summaries, conclusions, or out-

looks where appropriate to conclude one theme and link to the next. As mentioned already, he shows the biochemical principles of signal transduction with examples, each one representing the best researched—and perhaps most important—systems. He goes into great depth in these and lays great importance on the functional and structural finesses of the signal pathways as well as to make the proteins involved easily discernable. The text is too “heavy” in some places, but it always returns to a general view and a biological context. Occasionally (and perhaps too rarely) the link between a biochemical dysfunction and the associated illness is made. It is clear what is already known and which questions remain open. Now and then the author also permits himself to make suggestions as to what must be the next research topic.

The limited scope of this book indicates that the author intended the book for readers already with a basic knowledge of biochemistry. As such, this book is suitable for advanced students. However, it is also recommended for everyone working in the area of signal transduction research, who should keep this book at hand for when they want to clarify a particular mechanism or connection again, and to get quick access to the most important original papers and review articles. The contents of this book provides what the author promises: After reading it, one will have met the prominent signal pathways in cells and understood the principles of cellular signal transduction.

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Operators and Promoters. The story of Molecular Biology and its Creators. By *Harrison Echols* and *Carol A. Gross*. University of California Press, Berkeley 2001. 466 pp., hardcover £ 45.00.—ISBN 0-520-21331-9

This is an unusual book. One of the authors, the lambda phage expert Harrison (“Hatch”) Echols, began work on the book six years before his death in 1992. In contrast to a normal textbook,

in which one sets out to present the current situation in a field, Echols wanted to describe the development of the ideas, methods, and experiments of molecular biology, and the scientists involved. His aim was to discuss, from his viewpoint, the ways of thinking and working of individual researchers who have contributed to progress in the field, which he had himself taken part in and observed. He was certainly familiar with that. In 1992, when he died, the manuscript was unfinished. However, he had asked his wife, Carol A. Gross, to finish and publish the book. She has now done that, although it has taken almost ten years to complete it. The main contribution of the resulting book lies in the description of the work up to about 1990 on understanding transcription and its control in *E. coli*.

There are ten chapters. The first is an introduction to the structure and function of DNA and proteins. Chapter 2 deals with the deciphering of the genetic code. The book contains sketches by Echols of the scientists whom he knew and liked. Many of these are not generally well known. It seems that Echols did not know Erwin Chargaff and Heinrich Matthaei personally, and consequently there are no sketches of them, and the descriptions of them are rather superficial.

The following chapter is concerned with gene control. Echols recounts that when, at a conference in Cold Spring Harbor in 1961, he asserted that the regulation of the synthesis of alkaline phosphatase in *E. coli* is positive, Monod sprang to his feet and shouted “No, No! All regulation is negative. We have similar mutants, but we know how to interpret them correctly.” He then quotes Mel Cohn as describing how, a year later, Monod said to him: “Mel, we were right all along”. Such stories, which would not be found in a normal textbook, give one food for thought.

Further chapters are concerned with DNA replication, transcription, RNA, and DNA recombination. Then there is a chapter in which Echols is on more familiar ground, concerned with the regulation of regulation. Here the world of lambda phages, Echols's speciality, is brought to life. He reports how, in 1968, he tried to persuade the lambda phage research community to put together all