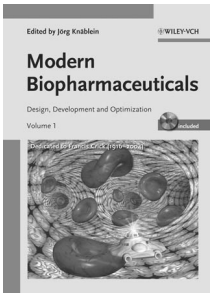
Biomolecular Drugs, Adrenergic Receptors

Modern Biopharmaceuticals: Design, Development and Optimization

By *Jörg Knäblein.*

Wiley-VCH, Weinheim 2005. CLXXXVII + 1886 pp., hardcover € 629.00.—ISBN 3-527-31184-X



The term "biopharmaceutical" apparently originated in the 1980s as a class of therapeutic products produced by modern biotechnological techniques. These incorporated protein-based products produced by genetic engineering or, in the case of monoclonal antibodies (mAbs), produced by hybridoma technology. Biopharmaceuticals can thus be described as proteins or nucleic acid-based pharmaceuticals, used for therapeutic or in vivo diagnostic purposes and produced by means other than direct extraction from a nonengineered biological source.

In 1982, the first biopharmaceutical, "humilin" (recombinant human insulin, produced in *Escherichia coli* and developed by Genentech in collaboration with Eli Lilly) was approved for use in the United States, thus initiating the biopharmaceutical industry. Since then the biopharmaceutical market has grown at an accelerating rate. More than 120 such products are now marketed around the world, including nine blockbuster drugs, which represent the mainstay products of the biotechnology industry. *Modern Biopharmaceuticals* is a four-volume work written to introduce readers to a comprehensive set of recently developed technologies that shows the paradigm shifts in the health care system and reflects these changes in industrial research. Jörg Knäblein, Head of Microbiological Chemistry at Schering AG, Berlin, Scientific Advisor, Executive Board Member, and President of the European Association of Pharmaceutical Biotechnology, and cofounder of the PharmaManagement Network, edited the work and coauthored one of the articles (*Production of Recombinant Proteins in Plants*, pp. 893–917).

The volumes are a truly international venture. The 186 world-renowned contributors are scientists and business leaders from academic, industrial, and governmental laboratories working in 17 countries: Germany, the United States, the Netherlands, Switzerland, the United Kingdom, Japan, Austria, Israel, Canada, Korea, Denmark, Poland, Spain, Australia, France, India, and Ireland, in the order of number of contributors. The four-volume set may be unprecedented in having such an eminent group of persons contribute to one biotechnology book. Three Nobel chemistry laureates, Robert Huber (foreword, *History of Modern Biopharmaceuticals: Where Did We Come From and Where Will We Go*, pp. xxxi–xxxiii), Thomas R. Cech (*Beginning to Understand the End of the Chromosome*, pp. 37–48), and Manfred Eigen (*Design of Modern Biopharmaceuticals by Ultra-high-throughput Screening*, pp. 583–603), are among the authors.

Several essays deal with controversial topics on the cutting edge of research, for example, *The First Cloned Human Embryo: An Unlimited Source of Stem Cells for Therapeutic Cloning* by Woo Suk Hwang et al. (pp. 269–281. On 20 March 2006, Hwang was dismissed from Seoul National University for fabricating data) and *Myocardial Regeneration Strategies using Human Embryonic Stem Cells* by Izhak Kehat, Oren Caspi, and Lior Gepstein (pp. 283–303).

The volumes are cumulatively paginated, printed on heavy, acid-free paper, and include numerous tables and figures, some in color and some full-page. The meticulously documented essays include references as recent as 2004. Each volume contains a table of contents (16 pp.) for the entire set.

Volume 1 (373 pp.) contains a prologue (3 pp.) and dedication (2 pp.) to Francis Crick, both by Knäblein; two forewords (3 and 2 pp., by Robert Huber and Günter Stock, respectively); four pages of quotes by Nobelists James D. Watson, Sir Aaron Klug, Stanley Cohen, Kary Mullis, and Paul Lauterbur as well as by Ian Wilmut ("clone-father of sheep Dolly"), Chris Walsh, and Detlev Ganten; and a list of contributors and their postal addresses (16 double-column pages). The most unusual and interesting introductory section in this volume is an extremely long (71 pp.) "Executive Summary" by Knäblein, which describes in detail each of the 75 signed and cross-referenced essays and thus provides a complete summary of the entire book's contents. *Current Status of Biopharmaceuticals: Approved Products and Trends in Approvals* (34 pp.), presents definitions, history, and lists of products, the companies producing them, therapeutic indications, and dates of approval. Extensive cross-references to essays in the book are given. *Biopharmaceuticals used in Molecular Medicine* includes 15 essays.

Volume 2 (342 pp., the shortest volume) contains *Biopharmaceuticals and their Mode of Action* (8 essays) and *Improving the Development of Biopharmaceuticals* (7 essays). Volume 3 (635 pp., the longest volume) consists of *Production of Biopharmaceuticals* (16 essays) and *Biopharmaceuticals Used for Diagnostics and Imaging* (9 essays). Volume 4 (471 pp.) contains *Advanced Application Routes for Biopharmaceuticals* (9 essays), *From Transcription to Prescription for Biopharmaceuticals* (5 essays), *From Bench to Bedside—the Aftermaths* (5 essays), an epilog (2 pp.), *More about the Editor* (2 pp.), and *Supplement CD–ROM* (4 pp.).

This final volume includes a detailed index (46 double-column pages) that facilitates location of information. Attached to the inside back cover is a supplementary CD–ROM disk with a PowerPoint presentation that the editor has used to share the fascination of biotechnology with students. It includes vivid video animations such as those showing the entire process from DNA unwinding in the nucleus through transcription into mRNA to the expression of a biopharmaceutical. By focusing on key aspects, the animations help one to understand such complex processes.

The next edition, which is intended to be even more comprehensive, is already in preparation, and Knäblein asks readers to suggest additional topics and content and to visit the biotechnology hub at his website http://www.get-gps.net to discuss current trends with a particular Global Pharma Specialist from a worldwide network.

I heartily recommend this authoritative, comprehensive reference to this new, exciting field dealing with the entire broad range of available biopharmaceuticals. It will be invaluable to biotechnologists, clinicians, physicians, pharmacists, pharmaceutical chemists, molecular biologists, medicinal chemists, and anyone working in the biotechnological and pharmaceutical industries or in medicinal institutes. It should also be useful for undergraduate and graduate students, postdoctoral fellows, and researchers seeking quick, clear, and concise ideas on topics outside their areas of specialization. It should also find a place in academic, industrial, and governmental libraries.

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The Adrenergic Receptors in the 21st Century

Edited by *Dianne M. Perez*.

Humana Press, Totowa 2005. 416 pp., hardcover $ 165.00.—ISBN 1-58829-423-4

The understanding of adrenergic receptors (AR) was initially driven by drug manipulation and tissue pharmacology. Now, molecular biology and the cloning of the receptors have completely revised the scientific approach to the structure, function, and pathophysiology of these receptors. To write a comprehensive book on this topic is a mundane task and requires many dedicated specialists. Dianne Perez has assembled a number of important contributors to the research area and grouped the 15 chapters into six parts. D. B. Bylund provides a brief historical *Perspective*, which is followed by Part II: Structure–Function. The chapter on *Ligand Binding, Activation and Agonist Trafficking* suffered most from an inadequate layout and poor graphical quality of the figures. Many graphics were carefully composed in colour, but here they appear in black and white. This makes them sometimes dull, sometimes hard to read. The compressed page layout with small margins and no breaks between sections is a real nuisance. More importantly, many chemical structures in this chapter are incorrect. Five structures out of 25 in Figure 4 are wrong. Two enantiomers are labelled (−)-epinephrine, and there is no link to the common name by which this is known. There is also an unusual use of italic annotation for amino acids (Table 1). Furthermore, references to the patent literature are missing, thus this chapter is far from comprehensive. Chapter 3: *New Signal Transduction Paradigms* addresses receptor dimerization and localization. A single figure is used to explain G protein-coupled receptors, their dimerization, and the associated signal transduction. Again, this figure suffers from poor layout and a "handcrafted" chemical structure. The oligomerization of GPCRs is missing altogether. The colour plates between Parts III and IV give an impression of what the book could have been and how much effort the authors have taken. Chapter 4 addresses the caveolae involvement in the *Regulation of the Cellular Localization and Trafficking of the Adrenergic Receptors* and is reasonably up to date. The confocal imaging of aortic smooth-muscle cells appears twice: on page 117 in black and white and some 50 pages later as one of the five colour plates. The *Clinical Medicine* in Chapter 5 consoled me. It is a concise overview, it highlights the problems and limitations, and finally makes a point for the experienced medicinal chemist in academia or the pharmaceutical industry. The following two chapters on visualization and localization of the adrenergic receptors by fluorescent-tagged ligands and receptors are comprehensive; they cover the literature up to 2004. The mouse models are addressed in five chapters grouped into Part IV. The topics are: α_1-AR and α_2-AR knockouts, β-AR knockouts, and AR overexpression and gene therapy. The positioning of pharmacogenomics in the closing Part V reflects the long history of AR research, which pharmacogenomics entered at a rather late stage in comparison with other receptors. The summarized polymorphisms, phenotypes, and their clinical relevance provide fertile ground for future individualized therapies. The necessary gene profiling is addressed in the last chapter: microarray analysis of novel AR function.

Medicinal chemists have to cherry pick from the chapters. Therefore, the book may not find the intended readership through this journal. On the other hand, many MDs, biologists, and pharmacologists will find the book rather appealing, as the receptor class is involved in numerous cardiovascular and pulmonary diseases.

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