Therapeutics of All Kinds

DNA Pharmaceuticals: Formulation and Delivery in Gene Therapy, DNA Vaccination and Immunotherapy

Edited by *Martin Schleef*.

Wiley-VCH, Weinheim 2005. xxii+253 pp., hardcover € 99.00.—ISBN 3-527-31187-4

As suggested by the subtitle, this book offers a fairly broad conspectus of what the Editor sees as a "completely new class of active pharmaceutical ingredients" involving the use of genetic material "for a preventive or curative application". It is conceived as the natural follow-up to Dr. Schleef's "Plasmids for therapy and vaccination" (Wiley-VCH, 2001), and is intended to take the reader "into the next step after design and manufacturing of plasmid DNA pharmaceuticals." We are told that "The focus is on the route of administration, quality control and regulatory aspects."

At this point the reader might be excused for thinking that this is a text aimed at scientist–entrepreneurs, involved in, starting up—or thinking about starting up—a new company in this area. And such specialists will indeed find the first few chapters valuable, particularly Chapter 2 on Regulatory Aspects and Chapter 3 on Plasmid Manufacturing and Storage. However, committed bench scientists, and the general reader, will be looking for a broader perspective. The good news is that they will not be disappointed. Most of the 13 chapters are written by practising academic scientists, and most offer a useful overview of a practical topic that most prospective readers will have heard of but few will have used themselves.

Chapter lengths vary widely with the subject matter, from just a handful up to 38 pages: so these are overviews rather than comprehensive reviews. However, the chapters are generally well-referenced: I looked first at the longest, Chapter 5, a well-written discussion with 324 references (into 2005) of "selected methods for localized nucleic acid delivery". This is a collaborative contribution from the Munich Technical University (Christian Plank and Franz Scherer, Department of Experimental Oncology) and the Children's Hospital of the Ludwig-Maximilian's University (Carsten Rudolph). The topics are well-chosen and well-organised, offering concise, practical, expert overviews of all the areas an interested reader might be looking for; plus several more that he might not be, but which might open a "serendipity channel". Anyone with a general interest in the area will appreciate the (two-page) introduction to nucleic acid delivery; the excellent, similarly brief summary of endocytosis and endosomal escape; and such authoritative, informative judgements as "It is still not well understood how and in what form nonviral vectors gain access to the nucleus." As might be expected, this particular topic is expanded later in the chapter, in well-informed discussions of localization and targeting (terms that are used synonymously). The chapter ends by introducing various physical methods of gene delivery (most of which are expanded upon in later chapters), with the pertinent reminder that drug–cell contact is typically driven by the physical process of diffusion, no matter how sophisticated the targeting apparatus.

The book's general emphasis, which may reasonably be seen as forward-looking, is on nonviral systems for DNA delivery into cells. When no delivery system is perfect, then simplicity becomes an important factor, and currently some 15% of gene-therapy trials involve naked DNA gene transfer. Thus "DNA vaccination" is a major topic, with separate chapters on Needle and Needleless Injection. The second longest chapter is a well-informed discussion of electrotransfection, followed by a chapter on its clinical applications. Hydrodynamic gene therapy is discussed briefly (in terms guaranteed to put off potential patients permanently). Other chapters deal with more specialized topics, some of which will be familiar, particularly those covering plasmid inhalation and treatment of skin diseases, where delivery is (superficially…) more straightforward and research correspondingly further advanced.

Technically the book is produced to the high standards we expect from this publisher. The format will be familiar to many readers, from the detailed lists of chapter contents and authors' affiliations and the (ever more essential) Table of Abbreviations, to the good 12-page index at the end. It makes a valuable contribution to an important, topical and rapidly growing area of research and will be useful and of interest to students and professors, specialists and beginners in the field. I recommend it strongly, to libraries and individual researchers, in areas ranging all the way from biological chemistry to medicine.

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Methods in Molecular Biology, Vol. 316: Bioinformatics and Drug Discovery

Edited by *Richard S. Larson*.

Humana Press, Totowa 2006. x+444 pp., hardcover $ 125.00.00.—ISBN 1-58829-346-7

It is almost impossible to begin this review without immediately pointing out that the title of this book inadequately describes the contents. About half of the chapters fit comfortably within the

scope implied by the title, including the several chapters on microarray methods and the chapters on gene ontology and gene evolution. Some of the material in the later chapters might be better described as cheminformatics, and the chapter on protein design is a slight stretch, but these are minor quibbles. The chapters that really stretch the limits of the title include those on mass spectroscopy and NMR methods for drug discovery. Another sprawling but enjoyable chapter ("Receptor-Binding Sites", by Darren R. Flower) includes, among other topics, X-ray crystallography, homology modeling, molecular dynamics, pharmacophore- and structure-based docking, pK_a prediction, and binding-site identification; only a few of these topics fit comfortably within a conventional, narrow definition of "bioinformatics". These chapters are well written and informative, and the book would be poorer without them. The editor finesses the issue of the title in the preface by defining the scope of the book to encompass "new, powerful technologies [for drug discovery] that have a prominent bioinformatic component". This statement would provide a more accurate, albeit awkward, title for the book. Whether the broad scope of the book is a strength or a weakness of this volume is, I suspect, a matter a taste. Bioinformaticists expecting to find in-depth discussions of topics more conventionally considered within the scope of their field might be disappointed. Readers looking for a broad overview of data-rich technologies for drug discovery will likely enjoy the volume quite a bit. By reading the whole volume, one can learn a great deal indeed.

The biggest strength of the book is that the chapters are written by active practitioners of the methods described, and the depth of their knowledge and enthusiasm are apparent. The overall feel of the book is a "from the trenches" view on various developing technologies for drug discovery. The detailed, step-by-step protocols distinguish this volume from other edited series. Lists of specific websites, and even examples of input files for specific analysis programs, are among the highlights. An inevitable corollary is that the focus on specific technology platforms narrows the scope; alternative programs/methods are sometimes omitted. Consistent with the broad scope of the book, roughly half of the detailed protocols describe experimental rather than computational techniques.

This compendium falls prey to common pitfalls of multiauthor volumes. There is considerable redundancy among the chapters, notably among the four chapters focused on microarray data, and among some of the later chapters that cover virtual compound libraries and their uses. The chapters also differ dramatically in style and organization. Some chapters are straightforward reviews of available technology. Some are case studies, highlighting how the authors have used bioinformatics and other technologies to solve a specific problem. The most satisfying are the chapters written as tutorials. Chapter 2, "Basic Microarray Analysis", written by Scott A. Ness, is a terse but lucid introduction to microarray methods, clearly written with non-experts (like myself) in mind. Chapter 14 is another short gem, providing a wealth of practical advice on chemical database preparation.

One final weakness of the book is the low quality of many of the figures. Many of the figures, particularly in the later chapters focused on structure-based methods for drug discovery, suffer from not being presented in color. In an age of elaborate Powerpoint presentations and color figures in essentially every journal, low-quality black-and-white images are jarring, and seem out of place in a reasonably pricey reference book.

After reading through the book, I find myself hoping that it will find a readership. The vast majority of titles in the *Methods in Molecular Biology* series describe experimental techniques. Introducing computational methods into this series is an important experiment, and I hope that other volumes will be forthcoming. The field of computational biology, including bioinformatics and other disciplines, can certainly benefit from an effort to reach out to a broad audience, by providing well-tested and -documented protocols that even novices can use profitably. This volume represents a worthwhile albeit imperfect step towards this goal.

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Directory of Therapeutic Enzymes

Edited by *Barry McGrath* and *Gary Walsh.*

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The editors address the book to biochemists working in biotechnological research in industry, research institutions and universities. The book provides a concise review of the recombinant enzymes produced for analysis and therapy. Particular focus is set on applied enzymology and enzyme engineering in the first two general chapters, which are followed by 11 chapters dealing in detail with selected examples of important enzymes used in therapies of blood-clotting disorders, in the treatment of cancer and some genetic disorders. Most of the authors of the 13 chapters are industrial experts, and their research areas cover genomics, protein biochemistry and analysis, biotechnology and clinical applications.

The use of recombinant enzymes in clinical therapy is a steadily growing field. It should be noted that very soon the first generica of products such as tissue plasminogen adivator will be on the market. Furthermore, about 100 enzymes are used as diagnostic tools. The industrial use of proteases and carbohydrates in food technology and in laundry and the leather industry will expand permanently. In particular, new thermostable and oxidant-resistant enzymes as well as enzymes working in organic media, for example, for group transformation of chemicals, will be developed. The bioengineering of novel properties is summarized in a special chapter.

The book describes recent research efforts and offers an up-to-date review of classical therapeutic enzymes, as shown

