Drug Discovery Research: New Frontiers in the Post-Genomic Era

Edited by *Ziwei Huang*.

John Wiley & Sons 2007. xviii + 521 pp., hardcover, $ 125.00.—ISBN: 978-0-471-67200-5

The wealth of information obtained from genomic sequencing endeavors has been a boon for scientists. Perhaps no field has benefited more than that of drug discovery. As a result, the identification and validation of targets has accelerated dramatically. Where would the field be in the absence of this abundance of data, and where has it taken us with respect to drug development? The goal of obtaining new pharmacological agents will surely continue to accelerate, yet it is often prudent to stop occasionally and assess the field as it stands. *Drug Discovery Research* does just that.

This book attempts to take a "snapshot" of the current efforts into the identification, evaluation, and improvement of drug leads through a diverse perspective, and attempts to deliver a taste of all the various studies being carried out. Indeed, a quick perusal of the table of contents demonstrates that the book maintains a broad overview of topics while also striving to preserve a bit of overlap to illustrate differing perspectives from scientists at the forefront of their fields. Importantly, the term "drug" is loosely defined and includes compounds used for the benefit of dissecting a biological pathway or protein in the field of chemical biology.

Part I serves as a blueprint for the identification of lead compounds by computational methods while also illustrating the use of these same methods for small-molecule improvement. Indeed, this section whittles down from an overview of docking and molecular modeling approaches to the more fine-tuned approach of selective screening of "targeted" small-molecule libraries. These chapters would be of major benefit to computational "newcomers". Part II provides biological examples that have and are benefiting from synthetic approaches. These include an excellent discussion on asymmetric synthesis, biocatalysis, purification, and ultimate activity of chiral compounds. Significant biological data on prepared compounds is presented which nicely dovetails into the synthesis of the structural analogues being constructed. Also included in this section is a nice description of α-helix mimetics, their use and construction. Their development begs the ultimate question: which portion of the mimetic has the potential to provide greater target specificity, the amino acids present in the parental α-helix, or the small-molecule appendages designed to "lock" their structure in place? An inclusion of a brief discussion of challenges faced by the immune response and methods for circumventing those challenges would be desirable here. Although these chapters are very specific on the application of methods to a specific target, many readers will identify the common themes that are applicable to other biological systems. Finally, Part III delves into the clinical relevance of small molecules and in vivo methods for assessing functional activity. Here, target pathways are illustrated as well as presentations of the complications arising from the disruption of protein function. Although the delivery of compounds is presented in Part II, I feel it fits more appropriately in this section.

This text serves to "open our eyes" about the power of the individual components and the complementary methods in the chain of development in drug discovery. It provides not only a summation of current computational, synthetic, and biological methods, but also provides the subtleties of the field, such as the newer use of neural stem cells in therapeutic intervention of severe disorders such as Parkinson's disease and the use of chemoenzymatic synthesis. The book should appeal to a broad range of scientists with an interest in the nuances of the world of drug development.

William A. Barton
Department of Biochemistry and Molecular Biology
Virginia Commonwealth University
Richmond (USA)
DOI: 10.1002/cmdc.200800016

Prodrugs: Challenges and Rewards. Parts 1 and 2

Edited by *Valentino J. Stella*, *Ronald T. Borchardt*, *Michael J. Hageman*, *Reza Oliyai*, *Hans Maag*, and *Jefferson W. Tilley*.

Springer, New York 2007. viii + 734 and ix + 730 pp., hardcover $ 599.00.—ISBN 978-0-387-49782-2

Most prodrugs are biologically inactive derivatives or analogues of drugs with insufficient oral bioavailability. Within the biological system they are activated by metabolic or chemical processes. Other prodrugs are designed to improve certain other properties such as solubility or taste, to enable permeation of the blood–brain barrier, or to achieve organ or cell selectivity. About 5–7% of all marketed drugs are indeed prodrugs, and their relative percentage is increasing.

In two volumes, the editors provide a comprehensive overview on early and current prodrug strategies. In addition to prodrugs that are marketed, many experimental approaches are described in detail. Almost every chapter includes an impressive collection of references, with publication years up to 2005. Volume 1 starts with an historical overview, followed by several chapters that describe problems to be addressed by prodrugs: permeability (three chapters), solubility (two chapters), metabolism (two chapters), controlled release (three chapters), and targeting to cancer, liver, brain, and colon (eight chapters). Volume 2 reviews prodrug approaches according to functional groups of drugs (nine chapters) as well as preclinical and clinical considerations (two chapters) and toxicological issues (two chapters). A most relevant and important section of Volume 2 covers case studies (252 pages in total); most of these 25 chapters are organized in sections on the rationale of prodrug design, synthesis, mechanism and site of bioreversion, toxicity, formulation, discussion, and conclusions.

Owing to the organization of the book, according to strategies in Volume 1 and functional group approaches and case studies, both in Volume 2, there is a significant overlap and much redundancy. The elegant

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim