Roleplay

Systems Biological Approaches in Infectious Diseases

Edited by *Helen I. Boshoff* and *Clifton E. Barry, III*.

Birkhäuser Verlag, Basel 2007. ix+349 pp., hardcover € 188.00.—ISBN 978-3-7643-7566-9

As witnessed in pharmaceutical industries, the problem of complexity in living systems is challenging the reductionism-based drug discovery techniques, and presently limiting the development of effective and safe drugs. Systems biology is expected to provide promising solutions to this challenge and to improve drug discovery and development in the post-genomic era. This book brings together various approaches in systems biology and demonstrates their applications to drug discovery in infectious diseases. All of the 12 chapters in this book showcase an emerging field using either practical examples from the various "omic" sciences or conceptual examples of how theories or models of living systems could contribute to drug discovery.

First, the current state of systems biology approaches in infectious disease is reviewed in Chapter 1. Then several popular "omics" platforms including transcriptome, proteome and metabolome are introduced in more detail in Chapters 2, 4 and 5, respectively. The data generated from these platforms have shown promise in revealing the mechanisms of pathogen–host interactions and anti-infectious drug actions, thus providing an opportunity to identify potential drug targets. A very interesting part of this book comes from the chapters that discuss the different approaches to identifying drug targets.

Chapter 3 introduces chemical genetic approaches to experimentally identify proteins responsible for a particular phenotype induced by drug perturbations. In contrast, Chapters 6–8 discuss ways to find novel targets computationally; for instance, a subsystem-based approach identified targets based on the essentiality and predicted vulnerability of the enzymes in the pathogens (Chapter 6), metabolic control analysis compared the flux through a single metabolic pathway in pathogen versus in host to identify vulnerable pathways (Chapter 7), and a protein-network-based method identified new drug targets by finding the proteins that linked directly or indirectly to current drug targets in the network (Chapter 8).

With increasing availability of data from various techniques, it has become possible to understand design principles of host–pathogen systems more accurately. In Chapter 10, a conceptual framework is proposed to understand and characterize the complex behaviors of host–pathogen systems in term of biological robustness. Chapter 11 discusses a constraints-based approach integrating available "omics" data and prior knowledge to model and simulate cell behaviors, thus allowing one to explore the dynamics of host–pathogen interactions. The last chapter describes functional genomics of host–pathogen interactions, which lends insight into the importance of gene acquisition and decay for pathogen evolution. These studies enable a better understanding of the principles of host–pathogen systems; therefore, they could provide valuable insights to guide the design of more effective therapeutics.

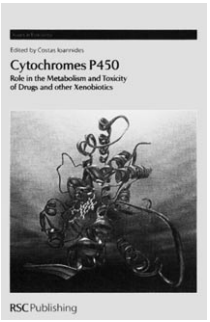
Overall, this book contains a mixture of reviews and specific methodological articles making for a somewhat uneven, but nonetheless very useful, compendium. The book is easily accessible and provides entry to newcomers into this field. The issues tackled by the book range from data generation to quantitative modeling of the various steps in the drug discovery process, including target identification and efficacy assessment, etc. Almost all of the approaches introduced in this book could be applied to other diseases, and are not limited to infectious diseases. Therefore many scientists in academia as well as pharmaceutical industries should find useful information in this book. However, it should be noted that this is a fast moving field, newly developed techniques and methodologies (i.e., next generation sequencing) relevant to this field are not covered in this book, thus interested readers should be encouraged to go to the literature for the latest progress in this field after reading this book.

Prof. Christina Chan, Dr. Xuewei Wang
Michigan State University (US)

Concerning Cytochromes P450: Role in the Metabolism and Toxicity of Drugs and other Xenobiotics

Edited by *Costas Ioannides*.

RSC, Cambridge 2008. xviii+522 pp., hardcover £ 110.00.—ISBN 978-085-404-2746



This book is one in a series entitled *Issues in Toxicology*, which is devoted to the coverage of modern toxicology and assessment of the risk. The book is a reference and guide to investigations in the biomedical, biochemical and pharmaceutical sciences at the graduate and post graduate level. The initiative for the book comes from the need to update the area of cytochrome P450, since it was some time

 © 2009 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

ago that a similar book was released. The publisher claims that the book should be of interest to scientists in the pharmaceutical industry, for regulators, and academic researchers and postgraduate students.

The book contains 15 chapters, written by 33 different authors, and is mainly divided into chapters covering each cytochrome P450 subfamily (CYP 1–4), as well as introductory chapters on the cytochrome P450 structure and function, reactive intermediates formed by cytochrome P450, and closing chapters covering their receptor-mediated regulation, the modulation of phytochemicals, and their role in cancer therapies. The chapters appear to have been written between October 2006 and November 2007, and essentially cover the literature published in 2006 and earlier. But what is new here that has not been presented before? A general update on the novel aspects of regulation, e.g microRNA and epigenetics, appear interesting. Furthermore, new cytochrome P450 genes have been described, in particular in animals. In fact, more than 5000 different cytochrome P450 sequences have been reported to date. Additionally, novel polymorphisms and alleles, and regulatory signal transduction pathways have been added. The toxicological aspects of this book, including metabolic schemes for drugs and other xenobiotics, have largely been published before in reviews and books, and consequently this book does not provide the reader with any new fresh information.

Overall, the book covers the cytochrome P450 field mainly from a historical and academic standpoint. The authors provide an overview of the basics of substrate specificities, inhibition, genetic polymorphisms and regulation of the different cytochrome P450 genes. The quality of the different chapters differs significantly. Some chapters mainly emphasize the author's own original research by reproduction of previously published data, whereas other authors indeed provide a novel updated aspect of their topic, including insights into fascinating developments in their field. Some chapters are short and not thorough enough. The different chapters take a different approach in describing the relative relationships in cytochrome P450s from human versus different animals; personally, this reviewer would have gained more from a generalized focus on human enzymes.

The book is merely encyclopedic in style rather than visionary and educational. It lacks summarizing figures and informative tables. In some cases, figures appear to have been copied from the internet sources, like the genomic website or the CYP allele nomenclature website. Additionally, a more critical attitude would have been beneficial to some of the authors describing, for example, results from genetic association studies and results from investigations in vitro to identify endogenous substrates for cytochrome P450s.

A wider discussion of clinical applications would have been attractive, and throughout the book there is a lack of applications to drug development. The chapter on cytochrome P450s in cancer therapeutics by Thomas Chang, however, contains such applications and I find it fresh and of interest. The chapter on receptor regulation by Paavo Honkakoski and others provides a very nice broad overview to the complex field.

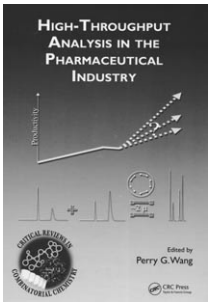
In summary, I consider the book an updated encyclopedia of the current situation in cytochrome P450 research, useful as a reference book in many laboratories both at universities and in industry. For such a purpose, it contains a rather large index and also several summarizing tables making it relatively easy to look up relevant information. For people with interest in a specific cytochrome P450 isoform, reading of the appropriate chapter will, in general, adequately provide the most important information regarding the cytochrome P450 in question, although for about 4–5 of the subfamilies, this book lacks some important information.

Prof. Magnus Ingelman-Sundberg
Karolinska Institute (Sweden)
DOI: 10.1002/cmdc.200900005

High-Throughput Analysis in the Pharmaceutical Industry

Edited by *Perry G. Wang.*

CRC Press, Boca Raton 2008. 432 pp., hardcover $ 159.95.—ISBN 978-1420059-53-3



The pharmaceutical industry is in the process of a major transition focused on increasing the effectiveness of drug discovery and development. The traditional timelines and budgets to bring new chemical entities to commercial viability are no longer acceptable. The industry requires increased productivity for the same amount of research dollars with a higher rate of research success. These increased expectations have stimulated researchers to find opportunities to reduce analytical cycle times in order to generate more analyses and provide greater information without significantly increasing their departmental budgets. Moreover, since decisions made in discovery tend to have an enormous impact on the success of programs in preclinical and clinical development, additional information regarding in vitro ADME and bioanalytical support of in vivo studies are expected to be part of the candidate nomination process.

The increased expectations for discovery have led to the need for automation and high-throughput analyses in order to keep up with the demand to generate more information. The book *High-Throughput Analysis in the Pharmaceutical Industry*, edited by Perry Wang, is an appropriate and timely contribution to the scientific literature. This book is a detailed review of the various analytical approaches that have been adapted for increased productivity in the pharmaceutical industry. The book is a compilation of manuscripts written by industry researchers that are presently engaged in the approach they are discussing, and offers valuable details and insights into each research area. Each manuscript is one of fifteen chapters and many of the

 © 2009 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim