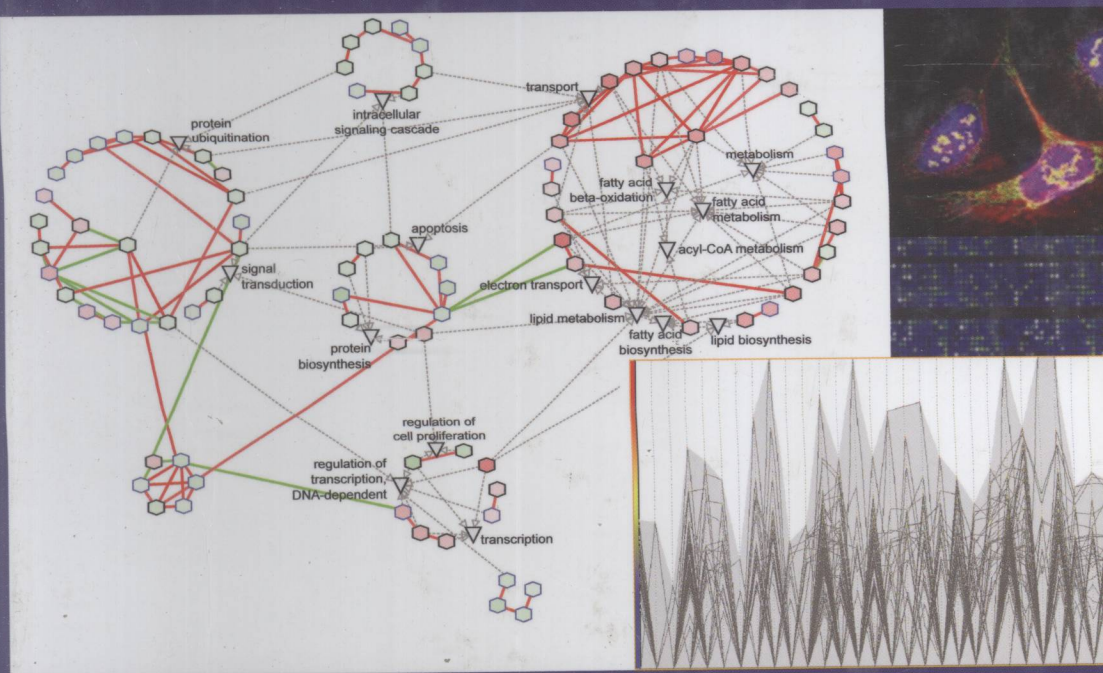


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Drug Efficacy, Safety, and Biologics Discovery

Emerging Technologies and Tools



Edited by **Sean Ekins and Jinghai J. Xu**

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DRUG EFFICACY, SAFETY, AND BIOLOGICS DISCOVERY

Emerging Technologies and Tools

SEAN EKINS
JINGHAI J. XU



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**DRUG EFFICACY,
SAFETY, AND
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DISCOVERY**

Wiley Series on Technologies for the Pharmaceutical Industry

Sean Ekins, Series Editor

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Drug Efficacy, Safety, and Biologics Discovery: Emerging Technologies and Tools

Edited by Sean Ekins and Jinghai J. Xu

To Enya, Elisa, and Penelope

Biotechnology is likely to be the main driving force of change in human affairs for the next hundred years.

Freeman J. Dyson, *A Many Colored Glass*, University of Virginia Press, 2007

Hopes of realizing the optimistic forecasts about the benefits that molecular biology will bring to pharmacology are likely, I believe, to be circumscribed by the state of physiological knowledge, models, and concepts.

Sir James Black, Foreword in *The Logic of Life*, edited by C. A. R. Boyd and D. Noble, Oxford University Press, 1993

PREFACE

Most drugs fail at the critical and expensive stage of clinical development due to inadequate prediction of efficacy and/or safety. Today new technologies that enable us to be more systematic and proficient at deciphering the complex interactions between biology and medicine are one of our best hopes in achieving a better therapeutic index. The goal of this book is to educate the readers in aspects of several key emerging technologies and how they have substantially impacted drug discovery, while stimulating thinking on how to better address safety and efficacy for drug research and development.

Systems biology, stem cells, RNAi, biomarker discovery and new models *in vivo*, are already influencing our predictions of drug efficacy. Automated data mining, computational (*in silico*) approaches, high-throughput screening and high-content screening, will continue to impact our predictions of drug safety. Finally, several key technological advances in nanotechnology, biologicals, and complex drug discovery will be presented in the same forum to foster the cross-fertilization of ideas between the fields of small molecule and larger molecule discovery. Indeed the breakdown of disciplinary silos and systematic application of the four modalities (manipulate, measure, mine, and model) are the central theme of this book. It is envisioned that the cross-disciplinary collaborations that are implicit in integrating these technologies with drug discovery operations will fuel the engine for future innovations. This book cuts across multiple areas of drug discovery. These areas are each presented by pioneers in the field, and they should have a broad appeal to many biological scientists and interdisciplinary technologists interested in drug research.

The book is not intended to be a *how to* book but rather to enhance knowledge of concepts and provide perspectives on drug discovery applications of

new technologies. Many of the chapters include case studies of how such technologies impact drug research and development. The reader should be able to take away from the book what the new technology is about, and how it enabled drug research and development that previous or conventional technology was not able to.

The book is divided into three sections:

Part I. Drug Efficacy and Safety Discovery

Part II. Biologics Technology

Part III. Future Perspective

Among the topics addressed are:

- High throughput protein-based technologies and computational models for drug development, efficacy, and toxicity.
- Systems pharmacology, biomarkers, and biomolecular networks.
- Computational systems biology modeling of dosimetry and cellular response pathways.
- Nanotechnology to improve drug delivery.
- Modeling efficacy and safety of engineered biologics.

The book's authors from pharmaceutical and biotechnology companies and academe have aimed to present an accessible volume for scientists at every level pursuing drug research and development. Each chapter has been edited to ensure consistency with explanatory figures and key references for readers who want to find out more about a topic. We hope that this book will prove to be a valuable reference resource on emerging technologies and tools and will enhance research productivity, which we show to be based on the modalities of manipulation, measuring, mining, and modeling.

ACKNOWLEDGMENTS

We sincerely thank Jonathan Rose and in particular Danielle Lacourciere, as well as and the team at Wiley for providing assistance and advice in developing this book. Our anonymous proposal reviewers are also kindly acknowledged for their helpful suggestions.

This book would not have been brought to fruition without the many authors of the chapters who agreed to contribute their time and effort in writing chapters. We thank them for allowing us to edit their work and making this such an enjoyable and rewarding endeavor.

J.J.X. would like to thank all his collaborators, teachers, and mentors in drug discovery and development. I am grateful to my parents and my family for encouraging me to follow my own path, and for being so supportive along the way.

S.E. would like to thank the editorial board and all the authors involved in creating this book series. I would like to acknowledge my family and Maggie for encouraging me to read, type, and pursue science topics of interest whenever I can.

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CONTENTS

PREFACE	ix
ACKNOWLEDGMENTS	xi
CONTRIBUTORS	xiii
PART I DRUG EFFICACY AND SAFETY TECHNOLOGY	1
1 Focus on the Fundamentals: Toward Better Therapeutic Index Prediction	3
<i>Jinghai J. Xu and Li J. Yu</i>	
2 High-Throughput Protein-Based Technologies and Computational Models for Drug Development, Efficacy, and Toxicity	29
<i>Leonidas G. Alexopoulos, Julio Saez-Rodriguez, and Christopher W. Espelin</i>	
3 Cellular Systems Biology Applied to Preclinical Safety Testing: A Case Study of CellCiphr™ Profiling	53
<i>Lawrence Vernetti, William Irwin, Kenneth A. Giuliano, Albert Gough, Kate Johnston, and D. Lansing Taylor</i>	
4 Systems Pharmacology, Biomarkers, and Biomolecular Networks	75
<i>Aram S. Adourian, Thomas N. Plasterer, Raji Balasubramanian, Ezra G. Jennings, Shunguang Wang, Stephen Martin, Jan van der Greef, Robert N. McBurney, Pieter Muntendam, and Noubar B. Afeyan</i>	

5	Zebrafish Models for Human Diseases and Drug Discovery	115
	<i>Hanbing Zhong, Ning-Ai Liu, and Shuo Lin</i>	
6	Toxicity Pathways and Models: Mining for Potential Side Effects	135
	<i>Sean Ekins and Josef Scheiber</i>	
7	Computational Systems Biology Modeling of Dosimetry and Cellular Response Pathways	155
	<i>Qiang Zhang, Yu-Mei Tan, Sudin Bhattacharya, and Melvin E. Andersen</i>	
8	Stem Cell Technology for Embryotoxicity, Cardiotoxicity, and Hepatotoxicity Evaluation	175
	<i>Julio C. Davila, Donald B. Stedman, Sandra J. Engle, Howard I. Pryor II, and Joseph P. Vacanti</i>	
9	Telemetry Technology for Preclinical Drug Discovery and Development	215
	<i>Yi Yang</i>	
PART II	BIOLOGICS TECHNOLOGY	229
10	Nanotechnology to Improve Oral Drug Delivery	231
	<i>Mayank D. Bhavsar, Shardool Jain, and Mansoor M. Amiji</i>	
11	Functional Glycomics and the Future of Glycomic Drugs	277
	<i>Ram Sasisekharan and Karthik Viswanathan</i>	
12	Modeling Efficacy and Safety of Engineered Biologics	301
	<i>Jeffrey R. Chabot and Bruce Gomes</i>	
13	Regulation of Gene Expression by Small, Non-Coding RNAs: Practical Applications	327
	<i>Roman Herrera and Eric Tien</i>	
PART III	FUTURE PERSPECTIVE	349
14	Future Perspectives of Biological Engineering in Pharmaceutical Research: The Paradigm of Modeling, Mining, Manipulation, and Measurements	351
	<i>Jinghai J. Xu, Sean Ekins, Michael McGlashen, and Douglas Lauffenburger</i>	
Index		381

PART I

DRUG EFFICACY AND SAFETY TECHNOLOGY