CONTENTS

CONTRIBUTORS ix
PREFACE xv

PART I BIOMARKERS AND THEIR ROLE IN DRUG DEVELOPMENT 1

1 Biomarkers Are Not New 3
Ian Dews

2 Biomarkers: Facing the Challenges at the Crossroads of Research and Health Care 15
Gregory J. Downing

3 Enabling Go/No Go Decisions 31
J. Fred Pritchard and Mallé Jurima-Romet

PART II IDENTIFYING NEW BIOMARKERS: TECHNOLOGY APPROACHES 41

4 Imaging as a Localized Biomarker: Opportunities and Challenges 43
Jonathan B. Moody, Philip S. Murphy, and Edward P. Ficaro

5 Protein Biomarker Discovery Using Mass Spectrometry–Based Proteomics 101
Joanna M. Hunter and Daniel Chelsky

6 Quantitative Multiplexed Patterning of Immune-Related Biomarkers 121
Dominic Eisinger, Ralph McDade, and Thomas Joos
7 Gene Expression Profiles as Preclinical and Clinical Cancer Biomarkers of Prognosis, Drug Response, and Drug Toxicity  
Jason A. Sprowl and Amadeo M. Parissenti  
135

8 Use of High-Throughput Proteomic Arrays for the Discovery of Disease-Associated Molecules  
Douglas M. Molina, W. John W. Morrow, and Xiaowu Liang  
155

PART III CHARACTERIZATION AND VALIDATION 177

9 Characterization and Validation Biomarkers in Drug Development: Regulatory Perspective  
Federico Goodsaid  
179

10 Fit-for-Purpose Method Validation and Assays for Biomarker Characterization to Support Drug Development  
Jean W. Lee, Yuling Wu, and Jin Wang  
187

11 Molecular Biomarkers from a Diagnostic Perspective  
Klaus Lindpaintner  
215

12 Strategies for the Co-Development of Drugs and Diagnostics: FDA Perspective on Diagnostics Regulation  
Francis Kalush and Steven Gutman  
231

13 Importance of Statistics in the Qualification and Application of Biomarkers  
Mary Zacour  
247

PART IV BIOMARKERS IN DISCOVERY AND PRECLINICAL SAFETY 287

14 Qualification of Safety Biomarkers for Application to Early Drug Development  
William B. Mattes and Frank D. Sistare  
289

15 Development of Serum Calcium and Phosphorus as Clinical Biomarkers for Drug-Induced Systemic Mineralization: Case Study with a MEK Inhibitor  
Alan P. Brown  
301

16 Biomarkers for the Immunogenicity of Therapeutic Proteins and Its Clinical Consequences  
Claire Cornips and Huub Schellekens  
323

17 New Markers of Kidney Injury  
Sven A. Beushausen  
335
PART V  TRANSLATING FROM PRECLINICAL RESULTS TO CLINICAL AND BACK  359

18  Translational Medicine—A Paradigm Shift in Modern Drug Discovery and Development: The Role of Biomarkers  361

19  Clinical Validation and Biomarker Translation  375
David Lin, Andreas Scherer, Raymond Ng, Robert Balshaw, Shawna Flynn, Paul Keown, Robert McMaster, and Bruce McManus

20  Predicting and Assessing an Inflammatory Disease and Its Complications: Example from Rheumatoid Arthritis  399
Christina Trollmo and Lars Klareskog

21  Pharmacokinetic and Pharmacodynamic Biomarker Correlations  413
J.F. Marier and Keith Gallicano

22  Validating In Vitro Toxicity Biomarkers Against Clinical Endpoints  433
Calvert Louden and Ruth A. Roberts

PART VI  BIOMARKERS IN CLINICAL TRIALS  443

23  Opportunities and Pitfalls Associated with Early Utilization of Biomarkers: Case Study in Anticoagulant Development  445
Kay A. Criswell

24  Integrating Molecular Testing Into Clinical Applications  463
Anthony A. Killeen

25  Biomarkers for Lysosomal Storage Disorders  475
Ari Zimran, Candida Fratazzi, and Deborah Elstein

26  Value Chain in the Development of Biomarkers for Disease Targets  485
Charles W. Richard, III, Arthur O. Tzianabos, and Whaijen Soo

PART VII  LESSONS LEARNED: PRACTICAL ASPECTS OF BIOMARKER IMPLEMENTATION  493

27  Biomarkers in Pharmaceutical Development: The Essential Role of Project Management and Teamwork  495
Lena King, Mallé Jurima-Romet, and Nita Ichhpurani
CONTENTS

28 Integrating Academic Laboratories Into Pharmaceutical Development
Peter A. Ward and Kent J. Johnson

29 Funding Biomarker Research and Development Through the Small Business Innovative Research Program
James Varani

30 Novel and Traditional Nonclinical Biomarker Utilization in the Estimation of Pharmaceutical Therapeutic Indices
Bruce D. Car, Brian Gemzik, and William R. Foster

31 Anti-Unicorn Principle: Appropriate Biomarkers Don’t Need to Be Rare or Hard to Find
Michael R. Bleavins and Ramin Rahbari

32 Biomarker Patent Strategies: Opportunities and Risks
Cynthia M. Bott and Eric J. Baude

PART VIII WHERE ARE WE HEADING AND WHAT DO WE REALLY NEED?

33 IT Supporting Biomarker-Enabled Drug Development
Michael Hehenberger

34 Redefining Disease and Pharmaceutical Targets Through Molecular Definitions and Personalized Medicine
Craig P. Webb, John F. Thompson, and Bruce H. Littman

35 Ethics of Biomarkers: The Borders of Investigative Research, Informed Consent, and Patient Protection
Heather Walmsley, Michael Burgess, Jacquelyn Brinkman, Richard Hegele, Janet Wilson-McManus, and Bruce McManus

36 Pathodynamics: Improving Biomarker Selection by Getting More Information from Changes Over Time
Donald C. Trost

37 Optimizing the Use of Biomarkers for Drug Development: A Clinician’s Perspective
Alberto Gimona

38 Nanotechnology-Based Biomarker Detection
Joshua Reineke

INDEX