Translational Medicine and Drug Discovery

This book, edited by two leaders known for driving innovation in the field, focuses on the new discipline of translational medicine as it pertains to drug discovery and development within the pharmaceutical and biotechnology industries. Translational medicine seeks to translate biological and molecular knowledge of disease and how drugs work into innovative strategies that reduce the cost and increase the speed of delivering new medicines for patients. This book describes these general strategies, biomarker development, imaging tools, translational human models, and examples of their application to real-life drug discovery and development. The latest thinking is presented by researchers from many of the world’s leading pharmaceutical companies, including Pfizer, Merck, Eli Lilly, Abbott, and Novartis, as well as from academic institutions and public–private partnerships that support translational research. This book is essential for anyone interested in translational medicine from a variety of backgrounds (university institutes, medical schools, and pharmaceutical companies) in addition to drug development researchers and decision makers.

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## Contents

**Contributors**  
**Preface**  
```
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>SECTION I: TRANSLATIONAL MEDICINE: HISTORY, PRINCIPLES, AND APPLICATION IN DRUG DEVELOPMENT</td>
<td>1</td>
</tr>
<tr>
<td>I. TRANSLATIONAL MEDICINE: DEFINITION, HISTORY, AND STRATEGIES</td>
<td>3</td>
</tr>
<tr>
<td>1.2. Pharmacology: Testing the Target (POM)</td>
<td>7</td>
</tr>
<tr>
<td>1.3. Study Design Considerations for POM</td>
<td>13</td>
</tr>
<tr>
<td>1.3.1. Population</td>
<td>13</td>
</tr>
<tr>
<td>1.3.2. Risk</td>
<td>14</td>
</tr>
<tr>
<td>1.3.3. Feasibility</td>
<td>14</td>
</tr>
<tr>
<td>1.3.4. Endpoints</td>
<td>15</td>
</tr>
<tr>
<td>1.3.5. PK–PD and PD–PD Models</td>
<td>16</td>
</tr>
<tr>
<td>1.4. Confirming the Hypothesis That a Drug Target (Mechanism of Action) Will Be Efficacious (POC)</td>
<td>17</td>
</tr>
<tr>
<td>1.5. Study Design Considerations for POC</td>
<td>17</td>
</tr>
<tr>
<td>1.5.1. Population</td>
<td>17</td>
</tr>
<tr>
<td>1.5.2. Efficacy Endpoints</td>
<td>19</td>
</tr>
<tr>
<td>1.5.3. Dose Selection</td>
<td>20</td>
</tr>
<tr>
<td>1.5.4. Cost, Speed, and Risk</td>
<td>20</td>
</tr>
<tr>
<td>1.5.5. Multiple Indications (Serial or Parallel)</td>
<td>21</td>
</tr>
</tbody>
</table>
## Contents

1. Human Indications Screening  
   1.6. Expl-IND Application  \(24\)  
   1.6. Low Cost Attrition and Portfolio Economics  \(26\)

1.7. Commercial Profile and Translational Medicine  
   1.7. Impact on Survival  \(27\)  
   1.7. Impact on Decision Making  \(29\)  
   1.7.3. Translational Medicine and the Personalized Medicine Option  \(31\)

1.8. Conclusion  
1.9. References  

### 2. TRANSLATIONAL MEDICINE AND ITS IMPACT ON DIABETES DRUG DEVELOPMENT

**Roberto A. Calle and Ann E. Taylor**  \(35\)

2.1. Introduction  
2.2. Primary Challenges  
   2.2. Efficacy  \(37\)  
   2.2. Safety  \(46\)

2.3. Case Studies  
   2.3.1. Case Study #1: Development of DPP-4i  \(49\)  
   2.3.2. Case Study #2: Development of 11-\(\beta\)-Hydroxysteroid Dehydrogenase Type 1 Inhibitors  \(50\)  
   2.3.3. Case Study #3: Effect of Weight Loss on HbA1c  \(54\)

2.4. Conclusions  
2.5. Acknowledgments  
2.6. References  

### 3. CHALLENGES IN ATHEROSEDROSCLEROSIS

**John S. Millar**  \(62\)

3.1. Introduction  
3.2. Prevailing Hypotheses of Atherosclerosis Development  
   3.2.1. The Lipid Hypothesis  \(62\)  
   3.2. The Response-to-Injury Hypothesis  \(63\)  
   3.2.3. The Response-to-Inflammation Hypothesis  \(64\)  
   3.2.4. The Response-to-Retention Hypothesis  \(64\)

3.3. Clinical Trials Supporting the Lipid Hypothesis  
3.4. Where We Stand Today  

### 3.5. Atherosclerosis and Drug Discovery and Development

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5.1. Lipoprotein Metabolism</td>
<td>67</td>
</tr>
<tr>
<td>3.5.2. Antidyslipidemics</td>
<td>69</td>
</tr>
</tbody>
</table>

### 3.6. The Future Generation of LDL-Lowering Drugs

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.6.1. Thyroid Receptor-β Agonism</td>
<td>73</td>
</tr>
<tr>
<td>3.6.2. Lipoprotein-Associated-Phospholipase A2 Inhibitors</td>
<td>73</td>
</tr>
<tr>
<td>3.6.3. Secretory Phospholipase A2 Inhibitors</td>
<td>74</td>
</tr>
<tr>
<td>3.6.4. Microsomal Triglyceride Transfer Protein Inhibitors</td>
<td>74</td>
</tr>
<tr>
<td>3.6.5. Antisense/RNA Interference of apoB mRNA</td>
<td>75</td>
</tr>
</tbody>
</table>

### 3.7. Therapies to Increase HDL Cholesterol Levels and Improve HDL Function

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.7.1. CETP Inhibitors</td>
<td>75</td>
</tr>
<tr>
<td>3.7.2. PPAR-α Agonists</td>
<td>76</td>
</tr>
<tr>
<td>3.7.3. Reconstituted and Recombinant HDL/apoA-I Mimetic Peptides</td>
<td>77</td>
</tr>
</tbody>
</table>

### 3.8. Biomarkers Linked to Clinical Outcomes

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.8.1. Biomarkers</td>
<td>77</td>
</tr>
<tr>
<td>3.8.2. Measures of Vascular Function and Atherosclerosis</td>
<td>78</td>
</tr>
</tbody>
</table>

### 3.9. Case Study: CETP Inhibition with Torcetrapib – Mechanism versus Molecule

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.10. Conclusion</td>
<td>80</td>
</tr>
<tr>
<td>3.11. References</td>
<td>82</td>
</tr>
</tbody>
</table>

### 4. OBESITY: NEW MECHANISMS AND TRANSLATIONAL PARADIGMS

**Gregory Gaich and David E. Moller**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1. Introduction</td>
<td>89</td>
</tr>
<tr>
<td>4.1.1. Medical Need and History of Failure</td>
<td>89</td>
</tr>
<tr>
<td>4.1.2. Pathophysiology and Principles of Energy Balance</td>
<td>90</td>
</tr>
<tr>
<td>4.2. Molecular Pathways and Associated Drug Targets</td>
<td>90</td>
</tr>
<tr>
<td>4.2.1. Central Regulation of Satiety-Thermogenesis</td>
<td>92</td>
</tr>
<tr>
<td>4.2.2. Modulating the Actions of Gut-Derived Peptide Hormones</td>
<td>96</td>
</tr>
<tr>
<td>4.2.3. Targeting Other Peripheral Pathways</td>
<td>98</td>
</tr>
<tr>
<td>4.3. Clinical Paradigm and Recent Clinical Experience</td>
<td>100</td>
</tr>
<tr>
<td>4.4. Translational Approaches</td>
<td>102</td>
</tr>
<tr>
<td>4.4.1. Target Engagement</td>
<td>103</td>
</tr>
<tr>
<td>4.4.2. Drug Pharmacology or Mechanism Biomarkers</td>
<td>104</td>
</tr>
</tbody>
</table>
### 4.4.3. Disease Process or Outcome Biomarkers and Mechanism Biomarkers Linked to Efficacy Outcomes 105

4.4.4. Subject Selection 106

4.4.5. Combination Therapy 107

### 4.5. Concluding Comments 107

### 4.6. References 108

---

#### 5. BONE DISORDERS: TRANSLATIONAL MEDICINE CASE STUDIES  S. Aubrey Stoch 115

5.1. Introduction 115

5.2. Challenges in Translational Research 116

5.3. Osteoporosis: Biomarker Considerations 116

5.3.1. Biochemical Biomarkers of Bone Turnover 116

5.3.2. Imaging Biomarkers (BMD) 118

5.3.3. Preclinical Models 119

5.4. Antiresorptives 121

5.4.1. Cat K Inhibitors 122

5.4.2. $\alpha_v\beta_3$ Integrin Antagonists 127

5.5. Osteoanabolics 130

5.5.1. Selective Androgen Receptor Modulators 131

5.5.2. Calcium Receptor Antagonists (Calcilytics) 136

5.5.3. Dickkopf-1 (DKK-1) Inhibitors 144

5.5.4. Sclerostin Inhibitors 149

5.6. Conclusions 155

5.7. References 158

---

#### 6. CASE STUDIES IN NEUROSCIENCE: UNIQUE CHALLENGES AND EXAMPLES  Gerard J. Marek 168


6.2. Why Have New Mechanisms Failed? 169

6.3. Can We Predict Efficacy in Short-Term Studies? 173

6.4. What Is the Role for Cognitive Biomarkers? 174

6.5. What Translational Medicine Approaches Will Drive Innovation in Neuroscience Drug Development? 175

6.6. References 177
7. TRANSLATIONAL MEDICINE IN ONCOLOGY  

**Dominic G. Spinella**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.1. Pharmacodynamic Biomarkers</td>
<td>180</td>
</tr>
<tr>
<td>7.1.1. Traditional Phase 1 Dose Selection versus the Paradigm for Targeted Agents</td>
<td>181</td>
</tr>
<tr>
<td>7.2. Outcome Biomarkers</td>
<td>183</td>
</tr>
<tr>
<td>7.3. Patient Selection Biomarkers</td>
<td>185</td>
</tr>
<tr>
<td>7.4. Putting It All Together: The Translational Approach</td>
<td>188</td>
</tr>
<tr>
<td>7.4.1. Preclinical Work</td>
<td>188</td>
</tr>
<tr>
<td>7.4.2. The Phase 1 Study</td>
<td>189</td>
</tr>
<tr>
<td>7.4.3. The Phase 2 Study</td>
<td>190</td>
</tr>
<tr>
<td>7.5. Conclusions</td>
<td>190</td>
</tr>
<tr>
<td>7.6. References</td>
<td>191</td>
</tr>
</tbody>
</table>

SECTION II: BIOMARKERS AND PUBLIC–PRIVATE PARTNERSHIPS

8. BIOMARKER VALIDATION AND APPLICATION IN EARLY DRUG DEVELOPMENT: IDEA TO PROOF OF CONCEPT  

**Pfizer Global Research and Development 2004**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1. Definitions and Summary of Overarching Principles</td>
<td>195</td>
</tr>
<tr>
<td>8.2. Biomarker Validation Terminology</td>
<td>197</td>
</tr>
<tr>
<td>8.3. Stages of Biomarker Lifecycle</td>
<td>198</td>
</tr>
<tr>
<td>8.4. Why Biomarkers?</td>
<td>200</td>
</tr>
<tr>
<td>8.5. Biomarker Validation</td>
<td>202</td>
</tr>
<tr>
<td>8.5.1. Define the Specific Purpose(s) of the Biomarker</td>
<td>202</td>
</tr>
<tr>
<td>8.5.2. Examine the Business Impact of Making a Wrong Decision</td>
<td>203</td>
</tr>
<tr>
<td>8.5.3. Select Appropriate Technical Validation Attributes</td>
<td>205</td>
</tr>
<tr>
<td>8.5.4. Create the Biomarker MAC and Appropriate Decision Criteria</td>
<td>209</td>
</tr>
<tr>
<td>8.5.5. Summary</td>
<td>214</td>
</tr>
<tr>
<td>8.6. When and How to Apply Biomarkers in Drug Development: Biomarker Development Is Described for Each Stage of Drug Development</td>
<td>215</td>
</tr>
<tr>
<td>8.6.1. Biomarker Development Must Occur So That Biomarkers Are Validated for Their Purpose Prior to Application for Drug Development Decisions</td>
<td>215</td>
</tr>
</tbody>
</table>
8.6.2. Biomarker Selection and Development between “Target Idea” and Decision on Drug Candidate Selection 216
8.6.3. Biomarker Best Practice between Drug Candidate Selection and First In-Human (FIH) Study 216
8.6.4. Biomarker Best Practice between FIH and Phase 2 Start 218

9. IMAGING BIOMARKERS IN DRUG DEVELOPMENT: CASE STUDIES Johannes T. Tauscher and Adam J. Schwarz 222

9.1. Introduction 222

9.2. Molecular Imaging: PET “Receptor Occupancy” as a Marker for Target Engagement 224
  9.2.1. A Brief History of Dopamine Receptor Occupancy with Antipsychotics 224
  9.2.2. Serotonin Transporter Occupancy with Antidepressants 226
  9.2.3. Case Study of a Translational PET Imaging Biomarker Strategy 227

9.3. Functional Imaging: fMRI as a Probe of Drug Effects in the CNS 228
  9.3.1. fMRI Biomarkers and Mechanistic Models in Early Drug Development 230
  9.3.2. Normalization of Brain Function: fMRI Studies in Patient Populations 233
  9.3.3. Validation and Standardization of fMRI for Drug Development Applications 234

9.4. Imaging as a Biomarker to Enrich Study Populations 235

9.5. Oncology 236
  9.5.1. Anatomical Imaging in Cancer Drug Development 236
  9.5.2. Functional Imaging in Cancer Drug Development 237
  9.5.3. Imaging the Tumor Vasculature 239
  9.5.4. Imaging of Cellular Proliferation 242
  9.5.5. Tumor Receptor Imaging 244
  9.5.6. Imaging Apoptosis 244

9.6. Imaging Cardiovascular Disease 245
  9.6.1. Clinical Trials in Atherosclerosis Using Imaging Endpoints 246
  9.6.2. Practicality of Cardiovascular Imaging Trials and Application to Drug Development 247
9.7. Conclusions 247
9.8. Conflict of Interest Statement 249
9.9. References 249

10. EUROPEAN NEW SAFE AND INNOVATIVE MEDICINES INITIATIVES: HISTORY AND PROGRESS (THROUGH DECEMBER 2009) Ole J. Bjerrum and Hans H. Linden 265

10.1. Introduction 265
10.1.1. The EU Research Funding System 265
10.1.2. Stakeholders 266
10.2. Toward the IMI 267
10.2.1. First Round: Establishment of the NSMF Project 267
10.2.2. Second Round: Incorporation of NSMF in FP 6 269
10.2.3. Third Round: The Rise of the IMI 271
10.3. Organizational Structure of the IMI 272
10.4. How Does the SRA of the IMI Address Predictive Markers of Efficacy and Safety? 274
10.4.1. Predictive Markers of Efficacy 274
10.4.2. Predictive Markers of Safety 276
10.5. How Is Off-Target Toxicity Addressed in the SRA? 277
10.7. The Topic Proposals in the First Call of the IMI 280
10.7.1. Predictive Safety 281
10.7.2. Predictive Efficacy 282
10.7.3. Knowledge Management 283
10.7.4. Education and Training 283
10.8. The Call Procedures 285
10.9. Future Perspectives 285
10.10. Acknowledgments 287
10.11. References 287

11. CRITICAL PATH INSTITUTE AND THE PREDICTIVE SAFETY TESTING CONSORTIUM Elizabeth Gribble Walker 289

11.1. Introduction to the Critical Path in Medical Product Development 289
11.2. The Predictive Safety Testing Consortium 290
11.3. Regulatory and Public Health Impact of the PSTC 292
11.4. References 293


David Wholley and David B. Lee 295
12.1. References 300

SECTION III: FUTURE DIRECTIONS 301

13. IMPROVING THE QUALITY AND PRODUCTIVITY OF PHARMACOMETRIC MODELING AND SIMULATION ACTIVITIES: THE FOUNDATION FOR MODEL-BASED DRUG DEVELOPMENT

Thaddeus H. Grasela, Jill Fiedler-Kelly, and Robert Slusser 303
13.1. Introduction 303
13.1.1. Chapter Overview 304
13.2. The Pharmacometric Analysis Process 304
13.2.1. The M&S Process in Pharmacometrics – Current Practice 305
13.2.2. The M&S Process in Pharmacometrics – Future Practice 306
13.2.3. The Central Role of the Franchise Disease–Drug Model 307
13.2.4. Implications of the Future Scenario 310
13.3. Challenges in the Delivery of M&S Results 311
13.3.1. Systematic Needs 311
13.3.2. Informatics Needs 312
13.3.3. Process Needs 313
13.4. Next Steps 314
13.4.1. Strategies for Improving the Quality and Productivity of the Pharmacometrics Process 315
13.4.2. Strategies for Improving the Quality and Robustness of the Informatics Infrastructure for Pharmacometrics 318
13.4.3. A Systematic Process for Assessing Franchise Disease–Drug Model Feasibility 319
13.4.4. Systematizing the Requirements Definition Management Process 322
14. EMBRACING CHANGE: A PHARMACEUTICAL INDUSTRY GUIDE TO THE 21ST CENTURY

Mervyn Turner

14.1. Introduction 328
14.1.1. Toward a New Paradigm of Drug Development 330
14.1.2. Embracing Democratization: Partner or Perish 331

14.2. Toward a New Paradigm of Drug Development: It's a State of Mind 331

14.3. Fail Fast, Fail Cheap 332

14.4. Philosophy in Action: Merck's Clinical Pharmacology and Experimental Medicine Strategies 334
14.4.1. Embrace Democratization – Partner or Perish 336
14.4.2. Adapt Culture to Recognize the Benefits and Necessities of Diversifying Pathways to Knowledge 337
14.4.3. Advance Experimental Medicine through Acquisition and Partnering 339

14.5. A Blueprint for Change 341

14.6. References 343

Index 345
Contributors

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Drug discovery and development has evolved in an accelerated fashion during the latter half of the 20th century and the first decade of the 21st century from the serendipity of folk medicine and herbal remedies to a more refined observational and hypothesis-driven biological approach and finally to the present-day translational approach that relies on an understanding of disease and human biology at a molecular level. Advances in information, molecular and biomarker technologies, and quantitative systems pharmacology have further enabled this rapid evolution. Along with these important advances and changes, however, has come an unsustainable attrition rate that has increased the cost of discovering and developing new drugs and threatens the future of the pharmaceutical industry as we have known it. The combination of modern, science-driven translational drug discovery and development and unsustainable attrition rates has created a new reality that has had its greatest impact on the earliest stages of drug development. This reality is mandating changes in strategies, technologies, and disciplines in an effort to improve confidence and the success rate of new drug targets, mechanisms, and molecules. Ultimately, these changes are designed to affect the endgame: improved productivity in terms of new drug approvals for unmet medical needs at a sustainable cost from the modern drug discovery engine.

One of the most significant changes embraced by the pharmaceutical and biotech industry is the creation and evolution of the discipline of translational medicine. We hypothesize that the successful implementation of translational medicine strategies will herald an era in which, from the initial decision to pursue a specific drug target forward, the line of sight is on proof of concept and not just the nomination of a drug development candidate. The effective use of biomarkers will enable development decisions regarding early drug candidates based on human drug target validation for the disease, pharmacodynamics, proof of mechanism, and proof of concept for the drug target and molecule. Specifically, biomarkers can be leveraged to define what constitutes adequate target engagement and as decision-making tools to confirm three hypotheses regarding the
target: (1) The relationship of target modulation to the biological changes that will result in a desirable effect in a disease population; (2) the ability of the compound to hit and modulate the target hard enough and long enough at a well-tolerated dose to test the concept; and (3) the level of efficacy and safety resulting from target modulation that is likely to be medically and commercially acceptable.

This book describes how the discipline of translational medicine has evolved to meet these drug development challenges and highlights current translational strategies and drug development paradigms across a diverse spectrum of therapeutic areas. Within Section I, experts define biomarkers and discuss the principles of the translational medicine discipline, describe the challenges and opportunities in translational paradigms unique to each disease area, and propose thoughtful solutions. Section II describes how biomarkers should be qualified to support the drug development process and how government and industry have responded to the needs and high costs of developing the tools and technologies required to develop new drugs efficiently and speed their delivery to patients. Finally, in Section III, we take a glimpse into the trends and changes needed for further success in the 21st century. An effort has been made in this volume to be transparent regarding cultural and management circumstances that must be dealt with and how companies should balance risk and drug development investments to be able to maximize the value from these translational medicine paradigms.

We expect that this volume will benefit drug discoverers and developers alike. Scientists in academia, regulatory institutions, and pharmaceutical industry laboratories, as well as those working on all aspects (chemistry, biology, physiology, pathophysiology, pharmacology, therapeutics) of translational discovery and clinical research, will find the book useful. Ultimately, we feel that it can serve as a useful training and educational tool for anyone interested in early drug development.

Bruce H. Littman, Stonington, CT
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