Target Discovery and Validation
Reviews and Protocols

VOLUME 2
Emerging Molecular Targets
and Treatment Options

Edited by

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Preface

During the last few years we have seen fundamental changes in the way scientists approach the identification and validation of new drug targets. These novel strategies for target validation are expected to maximize the likelihood of achieving target-selective inhibition with minimal in vivo side effects. For example, by the use of small interfering RNAs (siRNAs) to down regulate expression of known genes, a number of therapeutic targets have been validated both in vitro and in vivo. The technologies developed to do this have not only yielded a significant number of drug targets but have influenced our understanding of gene function, the molecular mechanisms of diseases, and the design of new therapeutic interventions. Specific gene and protein targets—on which, for example, cancer cells depend—can now be identified, along with the therapeutic agents directed against them. Several relevant examples that have been validated, and some that have reached the clinic, are featured in Volume 2, *Emerging Molecular Drug Targets and Treatment Options*, of *Target Discovery and Validation Reviews and Protocols*.

Despite knowing the molecular mechanisms of most drugs, patients vary in their responses to a medication’s efficacy and side effects. Indeed, the sequence of the human genome has shown that there is extensive genetic variation among individuals that would be expected to affect the response to medication. Thus, a better understanding of the molecular mechanisms that lead to an improved treatment response should play an important role in the development of individualized medicine. DNA sequence alterations and the expression profiles of mRNA molecules and proteins can be used to predict drug response. These genetic and epigenetic changes may be used in turn to develop treatment algorithms adjusted for use in individual patients. Several examples of such individualized treatment, aimed at increasing drug efficacy as well as decreasing toxicity, are discussed in this edition.

In systemic autoimmune diseases, current clinical practice calls for immunosuppressive drug therapy. However, some drugs are not target-specific and some carry a high risk of side effects. New immunosuppressive strategies, such as monoclonal antibodies and receptor antagonists, are now emerging as potentially valuable discriminating agents for use in innovative combinations. Such novel opportunities for therapeutic targeting in systemic autoimmune diseases are described in Volume 2.

MicroRNAs (miRNAs) are a family of short noncoding regulatory RNA molecules expressed in a variety of different cell types. These tiny RNAs have
been shown to play important biological functions and may regulate the expression of more than 30% of human genes. Presently, evidence is emerging that particular miRNAs may play a role in human cancer pathogenesis. Thus, the identification of miRNA expression signatures in patients with cancer may help to identify subjects who are at high risk of developing cancer or those who have an early stage of cancer. In order to interfere with miRNA expression, modified antisense oligonucleotides targeting individual miRNAs have been developed and these agents have the potential to eventually progress into a new class of therapeutic agents.

Volume II, *Emerging Molecular Drug Targets and Treatment Options*, was written by leading experts in the field and presents a unique source of current information. Along with Volume I, *Emerging Strategies in Drug Targets and Biomarker Discovery*, this work will be of interest to researchers, pharmaceutical companies, clinicians, and students of biology, medicine, or pharmacy.

I would like to thank the authors for their contributions, Anne Dybwad for critical reading of the manuscripts, and all those involved in the production of the book.

*Mouldy Sioud*
Contents

Preface .................................................................................................................. v
Contributors ........................................................................................................ ix
Contents of Volume 1 ............................................................................................ xiii

1 Druggable Signaling Proteins
   Mouldy Sioud and Marianne Leirdal .............................................................. 1

2 DNA Methylation and Histone Modifications in Patients With Cancer: Potential Prognostic and Therapeutic Targets
   Michel Herranz and Manel Esteller ................................................................. 25

3 Wnt Signaling as a Therapeutic Target for Cancer
   Andreas Herbst and Frank Thomas Kolligs .................................................. 63

4 The NG2/HMP Proteoglycan as a Cancer Therapeutic Target
   Martha Chekenya and Heike Immervoll ...................................................... 93

5 Heterotrimeric G Proteins and Disease
   Øyvind Melien ............................................................................................... 119

6 High-Mobility Group Box-1 Isoforms as Potential Therapeutic Targets in Sepsis
   William Parrish and Luis Ulloa ..................................................................... 145

7 Antisense Oligonucleotides: Target Validation and Development of Systemically Delivered Therapeutic Nanoparticles
   Chuanbo Zhang, Jin Pei, Deepak Kumar, Isamu Sakabe, Howard E. Boudreau, Prafulla C. Gokhale, and Usha N. Kasid ............................................. 163

8 Nucleic Acid-Based Aptamers as Promising Therapeutics in Neoplastic Diseases
   Laura Cerchia and Vittorio de Franciscis ....................................................... 187

9 Guidelines for the Selection of Effective Short-Interfering RNA Sequences for Functional Genomics
   Kumiko Ui-Tei, Yuki Naito, and Kaoru Saigo ............................................... 201
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Suppression of Apoptosis in the Liver by Systemic and Local Delivery of Small-Interfering RNA &lt;br&gt;<strong>Lars Zender and Stefan Kubicka</strong></td>
</tr>
<tr>
<td>11</td>
<td>Target Validation Using RNA Interference in Solid Tumors &lt;br&gt;<strong>Seyedhossein Aharinejad, Mouldy Sioud, Trevor Lucas, and Dietmar Abraham</strong></td>
</tr>
<tr>
<td>12</td>
<td>Validation of Telomerase and Survivin as Anticancer Therapeutic Targets Using Ribozymes and Small-Interfering RNAs &lt;br&gt;<strong>Nadia Zaffaroni, Marzia Pennati, and Marco Folini</strong></td>
</tr>
<tr>
<td>13</td>
<td>Collagen-Induced Arthritis in Mice: A Major Role for Tumor Necrosis Factor-α &lt;br&gt;<strong>Richard O. Williams</strong></td>
</tr>
<tr>
<td>14</td>
<td>Novel Opportunities for Therapeutic Targeting in Systemic Autoimmune Diseases &lt;br&gt;<strong>Meryem Ouarzane and Moncef Zouali</strong></td>
</tr>
<tr>
<td>15</td>
<td>Considerations for Target Validation and Industrial Approaches &lt;br&gt;<strong>Carlos R. Plata-Salamán and Sergey E. Ilyin</strong></td>
</tr>
<tr>
<td>16</td>
<td>Regulatory RNAs: Future Perspectives in Diagnosis, Prognosis, and Individualized Therapy &lt;br&gt;<strong>Marjorie P. Perron, Vincent Boissonneault, Lise-Andrée Gobeil, Dominique L. Ouellet, and Patrick Provost</strong></td>
</tr>
<tr>
<td>17</td>
<td>Treatment Options and Individualized Medicine &lt;br&gt;<strong>Mouldy Sioud and Øyvind Melien</strong></td>
</tr>
</tbody>
</table>

Index | 341 |
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## Contents of Volume 1:
*Emerging Strategies for Targets and Biomarker Discovery*

1. Main Approaches to Target Discovery and Validation  
   **Mouldy Sioud**

2. Bioinformatics Approaches to Cancer Gene Discovery  
   **Ramaswamy Narayanan**

3. Analysis of Gene Networks for Drug Target Discovery and Validation  
   **Seiya Imoto, Yoshinori Tamada, Christopher J. Savoie, and Satoru Miyano**

4. Target Discovery and Validation in Pancreatic Cancer  
   **Robert M. Beaty, Mads Gronborg, Jonathan R. Pollack, and Anirban Maitra**

5. Molecular Classification of Breast Tumors: Toward Improved Diagnostics and Treatments  
   **Therese Sørlie**

6. Discovery of Differentially Expressed Genes: Technical Considerations  
   **Øystein Røsok and Mouldy Sioud**

7. Genome-Wide Screening Using Small-Interfering RNA Expression Libraries  
   **Sahohime Matsumoto, Makoto Miyagishi, and Kazunari Taira**

8. Hammerhead Ribozyme-Based Target Discovery  
   **Masayuki Sano and Kazunari Taira**

9. Production of siRNA and cDNA-Transfected Cell Arrays on Noncoated Chambered Coverglass for High-Content Screening Microscopy in Living Cells  
   **Holger Erfle and Rainer Pepperkok**

10. Transgenic Animal Models in Biomedical Research  
    **Louis-Marie Houdebine**
11 Keratin Transgenic and Knockout Mice: Functional Analysis and Validation of Disease-Causing Mutations
Preethi Vijayaraj, Goran Söhl, and Thomas M. Magin
12 The HUVEC/Matrigel Assay: An In Vivo Assay of Human Angiogenesis Suitable for Drug Validation
Dag K. Skovseth, Axel M. Küchler, and Guttorm Haraldsen
13 A Murine Model for Studying Hematopoiesis and Immunity in Heart Failure
Per Ole Iversen and Dag R. Sørensen
14 An Overview of the Immune System and Technical Advances in Tumor Antigen Discovery and Validation
Mouldy Sioud
15 Potential Target Antigens for Immunotherapy Identified by Serological Expression Cloning (SEREX)
Dirk Jäger
16 Identification of Tumor Antigens Using Proteomics
François Le Naour
17 Protein Arrays: A Versatile Toolbox for Target Identification and Monitoring of Patient Immune Responses
Lina Cekaite, Eivind Hovig, and Mouldy Sioud