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.

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