Preface

Target discovery is a field that has existed for several years but is so vibrant today because of the recent progress in our understanding of the molecular mechanisms of many human diseases and the technical advances in target identification and validation. More sophisticated gene profiling technologies, such as DNA microarrays and serial analysis of gene expression, permit rapid identification of lead targets. Moreover, analysis of gene networks in living organisms allows the identification of target genes that operate in defined physiological pathways. With the sequencing of several genomes completed and the rapidly growing gene expression databases, there is now greater impetus than ever before for *in silico* discovery of therapeutic targets. Also, recent advances in genetic technologies have increased our ability to generate mouse models for human diseases. The implications of these genetically modified animals in drug development are several, including identification of new drug targets, predicting efficacy, and uncovering possible side effects. Together, these recent technical advances should allow researchers to make the most informed choice early and advance the chosen targets toward clinical studies.

Regarding cancers, any difference between a cancer and a normal cell could potentially be exploited as a therapeutic target. The hope is that drugs targeting specific constituents or pathways in cancer cells will provide more effective therapy, either alone or in combination with other currently used anticancer drugs. In addition to drug targets, identifying new target antigens remains as much of a challenge as improving tumor vaccines already in the clinic. New techniques such as SEREX, phage display, proteomics, and reverse immunology have not only yielded a significant number of new tumor antigens, but they have influenced our understanding of the interaction between the immune system and tumor cells. New adjuvants to improve vaccine potency are also being discovered.

Validating potential drug targets is one of the most critical steps in drug discovery. At present, the currently available target identification technologies appear to yield too many targets. Therefore, programs need to focus on defining the targets that are specific and "druggable" with small inhibitors. While true target validation comes only when a selective inhibitor for the chosen target is tested in patients and exhibits efficacy in the appropriate human disease, the appropriate cell culture and animal studies prior to the trial are not only required but should provide crucial information regarding the validity of the chosen tar-

get. Approaches to target validation might involve the use of small interfering RNAs, antisense oligonucleotides, antibodies, or engineered transgenic or knockout mice. Notably, several human diseases such as cancers and autoimmune disorders can be modeled in the mouse, making it an ideal tool to accelerate the validation process of new agents and the assessment of risk and toxicity.

Because of the rapid technical progress in the target discovery and validation field, we decided to divide *Target Discovery and Validation Reviews and Protocols* into two separates books, each describing specific topics. Volume 1, *Emerging Strategies for Targets and Biomarker Discovery*, provides the recent technological advances for the identification of molecular drug targets, biomarkers, and tumor antigens. In addition, it describes the role of knockout mice in functional genomics and target validation, as well as the clinical impact of gene expression profiling on oncology diagnosis, prognosis, and treatment. Volume 2, *Emerging Molecular Targets and Treatment Options,* concentrates on target validation strategies and on efforts to bring agents against specific targets closer to clinical application. We are presenting very up-to-date overviews and protocols by experts in the field. The covered topics will be of interest to researchers, pharmaceutical companies, and clinicians interested in developing or using new therapies. In addition, *Target Discovery and Validation Reviews and Protocols* will assist academic clinicians and students of biology, medicine, or pharmacy to appreciate the progress of the past few years in our understanding of cancer pathogenesis, cell signaling, gene profiling approaches, tumor immunology, tumor immunoediting, and immune tolerance.

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 *Target Discovery and Validation Reviews and Protocols.*

Mouldy Sioud