Preface

For the first time in the published literature, *Pharmacogenomics: Methods and Protocols* describes the newest and most commonly adopted technologies in the field of pharmacogenomics, providing guidance for investigators in the selection and experimental application of such technologies. Many of the contributors to this book are leading experts in the field. Using the extensive information provided on materials and methods, investigators will be able to easily reproduce each technique in their laboratories. Moreover, this book highlights problems that might be encountered in performing specific techniques and describes how to identify and overcome them. Pharmacologists, geneticists, molecular biologists, and physicians in academic institutions and the biotechnology and pharmaceutical industries will find *Pharmacogenomics: Methods and Protocols* an essential reference.

Pharmacogenomics exists at the intersection of pharmacology and genomics. It aims to study the genetic basis of interpatient variability in response to drug therapy. Pharmacogenomics holds the promise that drugs may eventually be tailor-made for individuals and adapted to each person's genetic makeup. Environment, diet, age, lifestyle, and disease state can all influence a patient's response to medicines, but understanding an individual's genetic makeup is thought to be the key to creating personalized drugs with greater efficacy and safety. Pharmacogenomics combines traditional pharmaceutical sciences with annotated knowledge of genes, proteins, and single nucleotide polymorphisms. Various technologies are currently available and researchers must be capable of choosing the technology suitable for their purposes.

After an introductory chapter about the history of pharmacogenomics and its current status, *Pharmacogenomics: Methods and Protocols* is divided in three parts. Part I comprises the methodologies for assessing the functional consequences of a certain polymorphism. Part II describes the variety of genotyping platforms currently available. Part III ends the book with two chapters devoted to the management of pharmacogenomic information.

A large amount of data about the pattern of human genomic variation has been provided by the Human Genome Project and is now publicly available. However, the functional consequences of SNPs and haplotypes are, for the most part, unknown, and current research efforts are oriented toward the elucidation of the genetic basis of changes in function of expression of the coded protein. Chapter 2 reports the classical method of transient expression combined with site-directed mutagenesis to study the functional effect of naturally occurring

variants in the UDP-glucuronosyltransferase 1A1 gene. Chapters 3–5 describe newer methodologies recently introduced to evaluate differences in gene expression between two genotypes/haplotypes. The allele-specific differential expression method described in Chapter 3 circumvents the analytic problems of confounding variation arising from environmental or physiologic factors during the analysis of subtle differences in expression between two different alleles. Chapter 4 provides a method for performing both genotyping and allele-specific gene expression for hundreds of genes using a chip system. Finally, it is crucial to take into account the haplotype structure of multiple variants when functional assays of single variants are performed. The HaploChIP is an in vivo cell-based assay that allows screening of haplotypes for differences in relative gene expression and is described in Chapter 5.

Part III deals with genotyping techniques. Chapters 6–13 present a wide variety of methodologies, platforms, and chemistries for genotyping. This section provides an understanding of the factors influencing the efficiency of different genotyping methods and the priorities required of different study designs. Readers will find technical information on several different types of assays, including denaturing high-performance liquid chromatography, pyrosequencing, kinetic-fluorescence detection assay, mass spectrometry, and TaqMan assay for insertion/deletions. Moreover, Part III describes the recent application in which genetic variation is surveyed in DNA pools from individuals enrolled in large studies.

The integration of genome-information management systems with patient clinical data sets is the key needed to achieve personalized medicine. Disparate data sources, including public or proprietary biology databases and laboratory and clinical information management systems, pose significant challenges in converting this information into clinically applicable knowledge. In Part IV, Chapter 14 describes PharmGKB, a registration-free interactive tool displaying genotype, molecular, and clinical primary data integrated with literature information and links to external sources. Finally, Chapter 15 gives an overview of the main technologies needed for the management of pharmacogenomic information.

I am extremely grateful to all the authors for their excellent contributions making this book a comprehensive and up-to-date resource for investigators in pharmacogenomics.

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