Preface

Heart disease and stroke are the leading causes of death worldwide (1). Atherosclerosis and hypertension are major risk factors for the development of heart disease and stroke, and kidney damage is an important risk factor for overall cardiovascular mortality. Despite the availability of medicines to ameliorate these illnesses, there remains a clear need for more effective therapies to reduce the global burden of cardiovascular disease.

One strategy for delivering improved therapies is deciphering the genes and cellular pathways that underlie cardiovascular disease. The last decade has brought tremendous advancement in technology for understanding the genome, including whole genome sequences of multiple species, platforms for high-quality measurement of genome-wide gene expression, high-throughput genotyping of single-nucleotide polymorphisms and copy number variations, as well as statistical packages for integrating phenotype information with genome-wide genotype and expression data. While these advances have led to better understanding of genome structure and function, the goal of identifying genes that cause cardiovascular disease remains distant. This is partly because linking genes with physiological function frequently requires combining genetic, physiological, bioinformatics, and statistical methods, a difficult task for most laboratories to achieve without collaboration. Therefore, the objective of this book is to provide methods for cardiovascular phenotyping of rodent models and for statistical and bioinformatic integration of phenotype data with genome-wide genotype and expression data. Understanding these diverse methods can allow an individual laboratory to utilize these genomic methods independently or to be better prepared to collaborate with scientists having expertise in other disciplines to uncover genes affecting cardiovascular disease.

Because mice and rats are the primary experimental species for genomic studies, Chapters 1–9 of the book focus on methods for evaluating cardiovascular phenotypes in these rodent models. Since some phenotyping methods, such as non-invasive and invasive blood pressure measurement, assessment of stroke, or echocardiographic evaluation of heart failure, are useful for evaluating both mice and rats, the protocols for both species are presented in the same chapter. Other methods, such as evaluating renal function and surgical induction of heart failure, have been commonly used in rat models, so chapters discussing these methods are focused on applying the protocol to mice. In the case of atherosclerosis, one chapter presents an experimental protocol for examining atherosclerosis in rats and a second chapter discusses how best to employ the various protocols that have been published for evaluating atherosclerosis in mice. Overall, the protocols presented in Chapters 1–9 should help investigators to reliably assess several important cardiovascular phenotypes in mouse and rat models.

Chapters 10–18 focus on statistical and bioinformatics methods for integrating phenotype data with genome-wide genotype and gene expression data. The first six chapters discuss statistical and computational methods for linkage mapping and
association studies, including single gene, genome-wide, and haplotype association studies, in experimental species or humans. These methods are important for mapping genes that underlie cardiovascular phenotypes. The subsequent chapters present bioinformatics methods for analyzing gene expression data from microarray studies and for linkage mapping of genome-wide gene expression in humans and rodents. The final chapter discusses a bioinformatics strategy for integrating phenotype, genotype, and gene expression data to identify the genes most likely to affect the phenotype of interest.

Combining the phenotyping protocols presented in Chapters 1–9 with the statistical and bioinformatics methods outlined in Chapters 10–18 will facilitate cardiovascular genomics studies in many laboratories. However, the statistical and bioinformatics methods described in Chapters 10–18 are not disease-specific and can be used for genomic analysis of most phenotypes. Hopefully, these protocols will enable researchers to identify causal genes and novel molecular targets that lead to new treatments for cardiovascular disease.

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Reference

Cardiovascular Genomics
Methods and Protocols
DiPetrillo, K. (Ed.)
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