PREFACE

With the postgenomic transcriptional era currently flourishing, the time seemed right to put together a book entitled *Cardiovascular Genomics*. Cardiovascular genomics is the study of genes relevant to the function and dysfunction of vital organs that both form and control the cardiovascular system. The book is organized into three parts: Part I: Genes and Polymorphisms in Cardiovascular Disease, Part II: Gene Transfer for Combating Cardiovascular Disease, and Part III: Regenerative Tissues for the Diseased Cardiovascular System.

Cardiovascular Genomics provides an up-to-date account of the most recent molecular approaches adopted to understand the cardiovascular system in both health and disease. The book provides an excellent resource for students, researchers, and clinicians on the potential of development of novel strategies for the control of cardiovascular diseases. The contributors are world leaders and the subject matter stretches from basic science to clinical applications, focusing on all components of the cardiovascular system—including vessels, heart, kidney, and the brain—and covers disease states ranging from vascular and cardiac dysfunction to stroke and hypertension.

Primary hypertension, a disease of the cardiovascular system, is a polygenic disease that has reached epidemic proportions worldwide. Most evidence suggests that susceptibility is genetically linked. Despite more than 50 years of using a large arsenal of antihypertensive agents, successful control of blood pressure is difficult to achieve. We believe this indicates that the time is ripe to explore alternate strategies. Cardiovascular genomics is all about doing just that. Discovering the genes that cause susceptibility to cardiovascular diseases will significantly increase the efficacy of treatment for these diseases. Remarkably, little is known about the numbers of genes involved in hypertension, what they do, their interactions with themselves and with others, and how they are modulated by stressors and diet, for example. *Cardiovascular Genomics* attempts to address these issues by focusing on both the villains and the victims.

Methods for identifying the genes that relate to a cardiovascular disease are discussed in relation to the possibility of discovering new drug targets. These approaches include discussions of genetic linkage analysis substitution mapping using congenic strains as well as microarray techniques. All are discussed as plausible strategies for discovery in animal models of hypertension. Not surprisingly, overactivity of the renin–angiotensin system may be one of the most common ailments and polymorphisms of angiotensin type 1 receptors and angiotensin-converting enzyme could well cause an overactivity of the signaling system. The new transgenic mouse models that either over- or underexpress angiotensinogen discussed within may help in addressing the important issue of the function of the tissue renin angiotensin systems. But an understanding of polymorphisms may also be crucial for the effective design of new drugs as well as successful pharmacotherapy for different patients; these important issues are thoroughly discussed, including those relating to statins.

A number of chapters in this book are dedicated to the theme of gene transfer and gene therapy covering a wide range of topics from clinical applications to using viral vectors as tools. For clinical applications, these include novel approaches to stroke, as well as

coronary and peripheral vascular diseases. The efficacy of gene therapy for safe gene delivery in cerebrovascular diseases has been used to stimulate angiogenesis, overexpression of vasodilator agents, or breakdown thrombi and stabilize plaques. These forms of somatic gene transfer have also been used to prevent both restenosis and vascular graft failure. Clear evidence has emerged that enhancing nitric oxide production reduces both oxidative stress and inflammatory responses that assist in lowering BP but also, independently, are beneficial in protecting against cardiac remodeling, renal fibrosis, restenosis and cerebral infarction as exemplified by adeno-associated viral-induced expression of kallikrein. In animal models of cardiovascular disease there are a number of chapters detailing a rapid expansion of viral vector technology in basic science. This includes applications to the heart, vasculature, and brain. The new strategies of virally mediated gene transfer include the design and effective use of expressing dominant negative proteins, siRNA, the employment of cell-specific promoters, and the use of vigilant vectors containing a physiologically operated genetic switch.

Cardiovascular Genomics also contains chapters on regenerative medicine that illustrate how molecular biology is enhancing the production of cardiovascular cells and tissues (e.g., cardiomyocytes and endothelial cells) from embryonic stem cells for repairing a diseased system. It is now clear that transplantation of genetically modified noncontractile cells into ischemic or dilated cardiomyopathic hearts can stimulate cardiomyogenesis that increases cardiac function. Moreover, regenerative medicine approaches now using ex vivo-engineered endothelial progenitor cells to treat peripheral and myocardial ischemia and genetically modified vein grafts have also proven successful.

The chapters in this book provide ample evidence for the considerable benefits that come from the application of genomic information and technologies to an understanding of both fundamental physiological processes and design of better therapies for one of the biggest killers worldwide. However, it is clear that many difficult challenges still lie ahead and must be confronted. Many methodologies and concepts are still evolving, common standards have yet to be established, and various problems with experimental design, variability, and statistical analysis still have to be fully understood and overcome. To fully realize the promise of the genomic approach, it is imperative that both scientists and physicians representing different disciplines work together to enhance progress. Only by means of multidisciplinary experimental approaches and the sharing of ideas can we develop novel cardiovascular therapeutics. Collaboration is the key that will unlock the genome.

The editors extend thanks to Ms. Nichole Herring for valuable assistance in putting together this volume.

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