
Preface

Since publication of the first edition of *Principles of Molecular Medicine*, dramatic discoveries in molecular medicine along with concomitant rapid technological advances have revolutionized the diagnosis and treatment of a broad range of human diseases. Given the pace of new discovery, genetic- and cell-based therapies may well become a common part of the physicians' armamentarium in the near future. Direct links between genetic mutations and diseases are being mapped almost routinely. Genomic approaches to diseases such as breast cancer have led to identification of previously unrecognized malignancies and the ability to prognosticate outcomes to therapy. The delicate interplay between adipocytes and regulation of insulin sensitivity, the roles of bone morphogenetic proteins in pulmonary hypertension, and the discovery of mutations involved in an array of cardiomyopathies are but a few of the important recent advances that have direct implications for patient care.

It is virtually impossible to keep track of the breadth of discovery that has led to these biomedical advances. The goal of the many authors and editors of this second edition of the *Principles of Molecular Medicine* has been to present the voluminous discoveries of the past decade in a format that captures the essence of scientific discovery but allows rapid assimilation in each particular area.

This second edition again includes chapters describing advances in fields paralleling traditional medical texts, and will be especially useful to specialists who are updating their education, practicing physicians interested in keeping abreast of new developments, and students appropriately curious about what is known and what lies ahead. Although only 8 years have passed since the first edition was published, we have made every effort to comprehensively update chapters with recent advances and have added chapters for disease entities and areas in which discovery has accelerated during the past five years.

As we have participated in the assembly of this volume, we have had the good fortune to review in depth the molecular discoveries that are transforming medical practice. For example, in the interval since the first edition of this text, stem cell populations have been discovered that regenerate muscle, heart, and neural cell populations, and that have the

potential to serve as cell-based therapies in chronic and degenerative diseases. New cell growth and cell death mechanisms that are dysregulated in neoplasia and that may serve as new anticancer targets have been elucidated. Advances have been made in understanding the biology of previously untreatable neurodegenerative diseases such as Huntington's disease. These and many other important advances in our understanding of human diseases are elucidated in this edition.

In addition, we have been able to note the new epistemologies in the genetic basis of human disease that are rapidly emerging. For instance, characterization of candidate genes for human diseases has expanded well beyond monogenic diseases, the study of late-onset diabetes being a notable example. Molecular alterations can have far-reaching effects on many systems. The identification of genes for epithelial sodium channels has led to a deeper understanding of their role in disorders of total body Na⁺ homeostasis, blood volume, and blood pressure. As a result of advances like these, views that had been held for much of the 20th century are being reconsidered. For example, hereditary hemochromatosis, a familial disease characterized by excess tissue deposits of iron leading to end-organ damage, has traditionally been thought to result from mutations in a single gene. Very recently, the identification of similar phenotypes associated with mutations of at least four different iron-metabolism genes has expanded our understanding of the pathophysiology of this relatively common genetic disease.

One common theme repeated in the chapters in this text is that the pathophysiology of disease is often a succession of genetic alterations, not just a single mutation. Although understanding these genetic relationships is never simple, their role in human diseases is all the more fascinating to consider. Human health often appears tenuous, but the discovery that a series of genetic missteps is often required to produce many disease states can be reassuring. The presence of several genetic steps in a disease process also suggests that multiple therapeutic targets may exist to modulate the course of these diseases. Less exhilarating is the knowledge that numerous diseases result not just from a complex succession of genetic missteps, but also from an individual's

interaction with the environment. Abundant examples of this principle are present throughout clinical medicine, and are described in detail in this edition of *Principles of Molecular Medicine*.

Paradoxically, as new discoveries are made, new mysteries appear. The many advances described in this volume often raise as many new questions as they answer. On the one hand, this indicates that biomedical discovery and medical practice will continue to evolve. On the other hand, the changes in medical care described in the chapters of this text are an indication that the unresolved questions of today may be harbingers of new therapeutic approaches in years to come.

It has been our pleasure to bring together in-depth expositions of the most recent advances in molecular medicine. We invite you to enjoy this magnificent point in biomedical history, as genetics and molecular medicine continue to merge with clinical practice. The compendium of information in *Principles of Molecular Medicine: Second Edition*, has been made possible by the tireless efforts of our section editors. Without their expertise and commitment to this project, this textbook would not be possible. In addition, we

thank the individual authors for sharing their expertise with all of us.

In addition to the phenomenal work of the editors and contributors, we would like to extend special thanks to Ms. Katie O'Brien for her commitment to this project; to Ms. Angela Clotfelter-Rego, whose tireless efforts despite numerous obstacles made this project possible; and to Ms. Carolyn Kruse, who synthesized the work of numerous authors to create a blazingly readable text. The editors thank our families, who have tolerated yet another joint effort. Finally, we would like to dedicate this volume to the first chairmen of medicine we had the privilege to serve under, Juha P. Kokko, MD, PhD, and Victor McKusick, MD. As physicians and scientists, these gentlemen nurtured many of the contributors to this edition, and their own work as scientists is frequently cited directly and indirectly in these chapters. It is on the shoulders of men like these that the principles of molecular medicine have been determined.

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