Book review

Post-Genomic Cardiology. Second Edition

Edited by José Marín-García. Academic Press; 2014: 924 pages, 84 tables and 194 figures. ISBN: 978-0-12-404599-6

Seven years ago, I was given the opportunity to review the first edition of this book, which was published in 2007. Dr. José Marín-García has updated and revised a new edition of that work. In these 7 years, we have been witnesses to the great surge in research into the genetic and molecular bases of cardiovascular disease. The use of "omics" has contributed enormously to this advance in the existing knowledge. The study of the genetic bases of diseases, building on linkage studies, genome-wide association studies, and genome sequencing (genomics), together with the new methods for studying gene expression (transcriptomics) and its regulation (epigenomics), advances in the quantification of proteins (proteomics) and their metabolites (metabolomics), the study of the molecular mechanisms that take place within the cell, such as signaling pathways and cascades, cell reprogramming, and the integration of all this information through the systems biology and the bioinformatics, have contributed to these advances. In this book, the author presents an ambitious review of all these aspects, focusing not only on genomic aspects, but on post-genomic aspects and their contribution to the current knowledge of the molecular bases of heart disease as well.

As I mentioned in my review of the earlier edition, the fact that the book was written by a single author, with the participation of three close associates, lends consistency and uniformity to the different chapters and facilitates their reading. Each chapter finishes with a highly useful summary that presents the main conclusions and the most important messages. The majority of the chapters provides a very extensive list of references (updated as of 2012), which facilitates the consultation of the original sources of the information. There are many tables summarizing the data and, in this new edition, the quality of the figures and graphs has improved quite notably.

The current edition has 11 well differentiated sections, each of which is divided into several chapters (between 1 and 5) that deal with different aspects related to the genomics of heart disease. With respect to the earlier edition, the contents have been updated and include new sections or chapters that are mainly related to the relevance of epigenetics and the mitochondrion to heart disease.

Section I offers a general introduction to the biochemical, cellular, and molecular functions of the heart under normal conditions. This section includes 3 chapters, the first 2 of which have been extensively rewritten. The 3 chapters introduce and review basic concepts related to gene structure, the processes of transcription and protein synthesis, and the cell cycle. The second chapter presents the methods for studying cardiac function at the molecular level, focusing on the different "omics". The last chapter of the section provides a review of the cell signaling pathways that regulate the growth, proliferation, and function of different cardiac cell lines. The author has updated the review of cell receptors and mitochondrial signaling, but the review of the intracellular pathways (adenyl cyclase, phospholipase, mitogen-activated protein [MAP] kinase, protein kinase, etc.), calcium signaling, and signals for cell cycle regulation, proliferation, and apoptosis has not been updated to any great extent in this second edition.

In section II, which is completely new, the author presents an excellent review, in 2 chapters, of the molecular mechanisms involved in embryonic heart development. In the first, he reviews the different signaling pathways and certain epigenetic factors that influence and regulate cell reprogramming in normal heart development; the second describes the known molecular changes that explain different congenital heart diseases.

Section III is the most extensive, with 5 chapters devoted to the analysis of arteriosclerosis, ischemic heart disease, angiogenesis, and hypertension. The first chapter describes the molecular mechanisms of arteriosclerosis and the second, the genetic bases of ischemic heart disease. In this second chapter, considerable weight is still given to evidence (often debatable) from linkage studies in family groups and from studies based on candidate genes. The author mentions genome-wide association studies, but only presents and discusses the results of the most important locus, located on chromosome 9 (9p21), but not the results at other loci. Another chapter reviews current knowledge on arterial and pulmonary hypertension but, again, does not include the contributions of genome-wide association studies, and there is no mention of existing knowledge about the genetic bases of lipid levels, a subject in which there have been notable advances in recent years. One example of the contribution of genetic knowledge concerning hypercholesterolemia to cardiovascular prevention, and its transfer to clinical practice, is the discovery of the *PCSK9* gene as the cause of some forms of familial hypercholesterolemia, the detection of a relationship between genetic variants of this gene and the risk of myocardial infarction, and the development of a new family of drugs, the anti-*PCSK9* antibodies. These antibodies have been shown to be effective in the control of cholesterol levels in patients with familial hypercholesterolemia, as well as in reducing the risk of coronary ischemic events (although the results are preliminary). This third section also includes a chapter on aspects related to cardioprotection and another that deals with angiogenesis.

Sections IV and V have also been extensively updated and restructured, and focus on the study of myocarditis, cardiomyopathies, and heart failure. They describe the genes and signaling pathways involved in cardiomyopathies (hypertrophic, idiopathic dilated, and restrictive cardiomyopathy and arrhythmogenic right ventricular dysplasia), in the cardiac response to inflammation and infection, and in the development of heart failure in patients with ischemic heart disease or hypertension. In this respect, the author has updated the content concerning ventricular remodeling, apoptosis and oxidative stress, and mitochondrial function in heart failure.

The book also reviews the molecular bases of arrhythmias, describing the genes involved in different channelopathies and in atrial fibrillation. The author presents and describes certain mutations than can be associated with a poorer prognosis in several heart diseases, although he admits that there are still many gaps in the current knowledge and, thus, cannot support their systematic utilization, and considers it necessary to continue to investigate the molecular mechanisms that regulate the different clinical presentations of a given genetic mutation.

Section VIII has only 1 chapter, which analyzes aspects related to sex differences in the context of cardiovascular diseases.

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The last 3 sections are very new and provide an exhaustive presentation of aspects related to the aging of the heart and cardiovascular system (3 chapters), the epigenetic mechanisms related to cardiovascular diseases, and possible new therapeutic horizons that all this knowledge is opening along the path toward personalized cardiovascular medicine.

In conclusion, as I commented with regard to the previous edition, this is a highly interesting book that focuses on molecular mechanisms related to different heart diseases, which undoubtedly can be of great utility to cardiologists and researchers in different areas (pharmacology, basic research, clinical practice, epidemiology) who are interested in these mechanisms.

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