

POST-GENOMIC CARDIOLOGY

Edited by José Marín-García. Academic Press, USA, 2007: 680 pages, 81 Figures, and 96 Tables. ISBN 978-1-4051-7362-9.

In recent years there has been a great boom in research into the genetic basis of different diseases, including cardiovascular diseases. Work has now even extended into the areas of gene expression and its regulation, including transcription (transcriptomics) and protein synthesis (proteomics), and to the study of the molecular mechanisms at work in cells, such as signaling routes and cascades. In this book, all aspects of the genomics of cardiovascular disease are reviewed. The author, José Marín-García, enjoys the help of just 2 collaborators—something quite unusual in these days of books written by many authors. This lends the book's chapters a sense of homogeneity that facilitates their reading. At the end of each chapter the reader will find a very useful summary of the main conclusions and messages. The majority of the chapters have an extensive bibliography (revised since 2005), making it easy for the reader to consult the primary sources used. The information discussed is summarized in the book's many tables, but the figures provided in the majority of the chapters are of low quality and could be improved.

The book has 10 well differentiated sections, each containing 1-5 chapters that discuss different aspects of the genomics of heart disease. The first section provides a general introduction to the biochemical, cellular, and molecular functioning of the heart under normal conditions. The 5 chapters of this section first review basic concepts related to gene structure, transcription, protein synthesis, and the cell cycle. They then go on to introduce the methods and laboratory techniques used in biochemical and molecular studies—from the analysis of DNA to the quantification of its expression, proteomic methods, and other technologies currently being developed. Also reviewed are the different techniques available for regulating gene expression in cardiomyocytes and endothelial cells in *in vitro* and animal models; the experience of their use in humans is also discussed. In chapter 4 the author discusses the techniques used in the *in vivo* study of cell functionality, the methods for culturing cell lines, and the transplantation of stem cells of different origin (embryonic, osteomuscular, from the bone marrow, and from heart myocytes, etc). Finally, the fifth chapter of this section provides an excellent review of the cell signaling pathways that regulate the growth, proliferation, and functionality of different heart cell lines, especially myocytes.

The second section has 2 chapters that together provide an interesting and exhaustive review focusing on pediatric cardiology. The first chapter discusses the present state

of the art of the molecular and genetic analysis of embryonic heart development. The factors that regulate the differentiation of the cardiac mesoderm, the cell signaling pathways involved in this process, the transcription factors that regulate the migration of cardiac precursors, those that take part in cardiac folding, the process of the definition of the right and left sides of the heart, and the formation of the heart chambers are all discussed. Also described are the different environmental factors that affect the development of the heart, including drugs, toxins, infections, etc. The second chapter of this section describes the main mutations known to be involved in different congenital heart diseases.

Section III is one of the longest, with 5 chapters devoted to the analysis of ischemic cardiomyopathy, angiogenesis, and high blood pressure. The first 2 chapters focus on the molecular basis of atherosclerosis, dyslipidemia, and thrombosis. Information is provided from linkage studies in family groups—studies that have allowed the different areas of the genome that might harbor genes involved in these abnormalities to be identified. Information from association studies on candidate genes is also provided. As the author points out, this information is controversial since it has not been reproduced in different populations.

Unfortunately, neither of these chapters make reference to the Hap-Map study which described the pattern of linkage disequilibrium (association) that exists between the different genetic markers in the genome, and which described the blocks containing markers strongly associated with one another. The genotyping of one of these markers thus reveals much of the genetic variability of the block to which it belongs. This information has allowed genome-wide association studies involving the genotyping of between 500 000 and 1 000 000 genetic markers in each person studied, covering 70%-80% of the genetic variability mentioned in the HapMap study. Studies of this type have been underway for about 2 years and have been very useful in identifying new genetic variants and genes associated with the risk of complex diseases, including ischemic cardiomyopathy. The National Human Genome Research Institute in the USA has a web page that publishes new results coming out of this kind of study (<http://www.genome.gov/26525384>). References are also missing on other cardiovascular risk factors, especially diabetes.

The following 2 chapters of this third section discuss the cellular and molecular pathways involved in the cardiac protection induced by ischemic conditioning, and the process of cardiac neovascularization is described. The last chapter reviews current knowledge on systemic high blood pressure and the mutations described to cause pulmonary hypertension.

The 2 following sections describe the genes and signaling pathways involved in cardiomyopathies (hypertrophic, dilated idiopathic and restrictive, and arrhythmogenic dysplasia of the right ventricle), in the heart's response to inflammation and infection, and in the appearance of heart failure in patients with ischemic cardiomyopathy and high blood pressure. The book also discusses the molecular basis of arrhythmias, describing the genes involved in long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and atrial fibrillation. Unfortunately these last sections lack information that might be of clinical use, such as a description of the mutations associated with poor prognosis in different heart diseases.

The last 3 sections of the book, with just 1 chapter each, also discuss—although not in great depth—features related to differences in sex, environmental factors, and the aging of the cardiovascular system.

In conclusion, this is a very interesting book that focuses on the molecular mechanisms involved in different heart diseases. Undoubtedly it will be of great use to cardiologists as well as researchers working in pharmacological, basic, clinical, and epidemiological fields with interests in these areas. The book centers on the description of these mechanisms and does not go deeply into the use of this knowledge in daily clinical practice. This limitation is probably not a fault of the author but of the fact that it is commonly very difficult to translate this information to the bedside. The development of new drugs and the identification of new diagnostic and prognostic markers etc. can take years of work—and may sometimes never bear fruit.

Roberto Elosua

Instituto Municipal de Investigación Biomédica,
Barcelona, Spain