

Preface

The concept of cardiac remodeling as a mechanism of heart disease leading to heart failure has evolved since the mid-1970s. The initial emphasis was on heart failure related to pressure and volume overload; this led to theories on adaptive and maladaptive structural and functional changes after life-threatening insults such as myocardial infarction and hypertensive heart disease. Later, the scope of cardiac remodeling expanded to pure and mixed pressure and volume overload states and a wide range of cardiomyopathies, inherited or acquired from infections or exposure to various therapeutic drugs with cardiotoxic pleiotropic effects and other cardiotoxic agents. Results of cardiovascular research at the bench and bedside levels and a host of population studies since the mid-1980s fueled the concept of adverse left ventricular remodeling during acute and subacute phases of myocardial infarction, with structural changes that have a negative impact on cardiac function. These studies have established that adverse cardiac remodeling is a major mechanism for progressive left ventricular enlargement, deterioration of ventricular function, increased suffering, and deaths from chronic heart failure. Concurrently over the last 4 decades, expanding knowledge of the basic molecular mechanisms and clinical implications of cardiac remodeling has identified several molecular pathways and potential targets, leading to drug discovery and development and improved therapies for major causes of adverse cardiac remodeling, such as myocardial infarction and hypertension. A major advance has been the appreciation that lifelong exposure to cardiovascular risk factors and cardiotoxic agents, beginning from the pediatric age through adulthood and old age, fuels the march to heart failure. This has opened up a new area of research into the biology of aging and its impact on cardiac remodeling.

Despite the advances, hearts continue to enlarge, and the heart failure burden continues to increase, especially after ST-segment-elevation myocardial infarction (STEMI). Many knowledge gaps exist. With the expanded spectrum of diseases that result in adverse cardiac remodeling, improved understanding of the underlying molecular mechanisms through research is crucial. During the last 20 years, attention focused on cellular and subcellular changes, including those at the molecular

and biochemical levels. There has been an explosion in knowledge of molecular and cellular mechanisms, importance of oxidative stress, metabolic pathways, extracellular and intracellular matrix remodeling, and the far-reaching effects of infarct and non-infarct zone fibrosis in the progression to heart failure. This has led to a profusion of original scientific and review papers dealing with several aspects of molecular mechanisms of adverse cardiac remodeling. There is therefore a need to synthesize these ideas into one book on molecular mechanisms of cardiac remodeling.

The main objective of this book has been to summarize the major research advances in molecular, biochemical, and translational aspects of cardiac remodeling over the last 2 to 3 decades under one cover and touch on future directions. The invited leaders and established investigators in the field have generously contributed 30 chapters on key topics relating to molecular mechanisms, with emphasis on selected biochemical and translational aspects of cardiac remodeling. The authors have succinctly summarized large volumes of data on these key topics and highlighted novel pathways and key molecules that need to be further explored and possibly targeted. They provide integrative reviews of the basic mechanisms and clinical correlates as well as critical assessments of publications on the key topics by the leading investigators in the field. The reference lists are fairly comprehensive and include key papers that are currently not easily accessed from Pubmed or other search engines. The book is carefully organized into two sections: Section A contains 15 chapters that focus mainly on molecular mechanisms in pressure and volume overload hypertrophy, with some overlap into brief ischemia–reperfusion injury; Section B contains 15 chapters that focus on molecular mechanisms after myocardial injury and infarction. The list of topics is by no means comprehensive but addresses some major areas needing attention. To our knowledge, there is no other book on this topic to date.

In summary, this book provides a high-profile and valuable publication resource on molecular mechanisms of cardiac remodeling for both the present and future generations of researchers, teachers, students, and trainees. It should stimulate future translational research targeted towards discovery and development for preventing, limiting, and reversing bad remodeling over the next few decades, with the ultimate goal of preventing progression to systolic and/or diastolic heart failure. The chapters suggest potential novel strategies that should receive attention for translating basic research knowledge to application in patients at the bedside. We would like to thank all the authors for their excellent contributions. We would also like to express our deepest appreciation for the preparation and editorial help provided by Catherine E. Jugdutt, Eva Little, and Dr. Vijayan Elimban in assembling this book. Cordial thanks are also due to Ms. Portia Formento and Melanie Tucker, Springer, USA, for their continuous advice and understanding during the editorial process. We hope that the book will prove useful for scientists and clinicians, students and teachers, and the industry interested in drug and discovery research.

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Cardiac Remodeling

Molecular Mechanisms

Jugdutt, B.I.; Dhalla, N.S. (Eds.)

2013, XI, 569 p. 78 illus., 46 illus. in color., Hardcover

ISBN: 978-1-4614-5929-3