



EDITED BY
W. MATTHIJS BLANKESTEIJN
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INFLAMMATION IN HEART FAILURE



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Preface

Heart failure is a progressive condition that affects an increasing number of patient worldwide and severely impairs their physical capabilities and quality of life. Despite large scientific efforts, the molecular mechanisms that lead to heart failure are still far from elucidated. Therefore, diagnosis of this condition is difficult unless the patient has reached a progressed state, accompanied with clinical symptoms. A better understanding of the molecular mechanisms contributing to the earlier phases of heart failure development would therefore help to improve the diagnosis and therapy. The drugs that are currently used can slow down heart failure progression but cannot cure the patient; moreover, the effectiveness of these interventions may very much depend on the subtype of heart failure, as many patients suffering from heart failure with preserved ejection fraction show little benefit from therapies with proven efficacy in heart failure with reduced ejection fraction.

An example of a molecular mechanism that is involved in the development and progression of heart failure is inflammation. It was originally observed in the wound-healing response that takes place in the area of injury after myocardial infarction. There, the inflammatory response is crucial for the removal of the necrotic debris from the area of injury and helps to attract the cells involved in the formation of a scar. In the meantime, inflammation has been described in cardiac remodeling due to other causes, for example, hypertension, and is already activated early on in its development. This highlights the importance of inflammation as a common molecular pathway of heart failure, providing potentially interesting options for diagnosis and therapy. However, the clinical results of interventions in inflammatory pathways have been disappointing so far, underscoring the complexity of the inflammatory response and the need for a better understanding of its molecular mechanisms. Therapeutic targeting of inflammation will therefore likely require careful patient selection and precise timing of the intervention to become successful.

The purpose of this book is to provide the latest information on the role of inflammation in heart failure to researchers and advanced students in the cardiovascular diseases. To this end, we have invited experts in the field to provide a comprehensive and timely overview of their research areas. The book is structured into three sections, providing the reader with easy access to the information. In Section 1, which focuses on the *pathophysiology of the inflammatory response in heart failure*, an overview is provided of the extensive literature on the role of inflammation in heart failure, with a distinction between ischemia-induced heart failure and heart failure due to other causes. Specific emphasis is put on the role of the innate immune system and the interaction between the extracellular matrix and the inflammatory mediators. The cross talk between the inflammatory response in the heart and the brain is highlighted and the section is finalized with an overview of different animal models of heart failure and their advantages and restrictions for the study of this condition.

In Section 2, the focus is on *inflammatory biomarkers*. The section starts with an overview of multiple inflammatory mediators as biomarkers for adverse remodeling and heart failure. Next, the pros and cons of different analytical techniques for measuring panels of inflammatory biomarkers in a single sample are discussed. In the last chapter of this section, an overview of imaging modalities to visualize the inflammatory response is provided.

Targeting of the inflammatory response is the subject of the third section of this book. Here, we focus on the experimental and clinical evidence for the beneficial effects of interventions on mineralocorticoid receptor and peroxisome proliferator-activated receptors. The modulating effects of statins and the involvement of miRNAs in the control of the inflammatory response and their therapeutic potential are discussed. Finally, the results of clinical trials with anti-inflammatory agents are presented and interpreted in light of our current understanding of the inflammatory response in heart failure.

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Raffaele Altara

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S E C T I O N 1

PATHOPHYSIOLOGY OF THE
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HEART FAILURE

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