

Preface

The heart has a very high energy demand but very little energy reserves. As a result, the heart has to continually produce a large amount of ATP necessary to sustain contractile function. The heart utilizes free fatty acids mainly and carbohydrates to some extent as substrates for making energy and any change in this energy supply can seriously compromise cardiac function. It has emerged that alterations in cardiac energy metabolism are a major contributor to the development of a number of different forms of heart disease. It is also now known that optimizing energy metabolism in the heart is a viable and important approach to treating various forms of heart disease.

This book describes the research advances that have been made in understanding what controls cardiac energy metabolism at molecular, transcriptional, and physiological levels. It also describes how alterations in energy metabolism contribute to the development of heart dysfunction, and how optimization of energy metabolism can be used to treat heart disease. The topics covered include a discussion of the effects of myocardial ischemia, diabetes, obesity, hypertrophy, heart failure, and genetic disorders of mitochondrial oxidative metabolism on cardiac energetics. The treatment of heart disease by optimizing energy metabolism is also discussed, which includes increasing overall energy production as well as increasing the efficiency of energy production and switching energy substrate preference of the heart.

The chapters are written by leaders in the field of research dealing with cardiac energy metabolism. The first part deals with how cardiac energy metabolism is controlled in the heart. The chapter by *Taegtmeyer* describes the role of carbohydrate metabolism in cardiac energy production whereas that by *Drosatos and Goldberg* presents an eloquent review of the role of lipoproteins in providing fatty acids and other essential lipids to the heart. This is followed up by a chapter by *Wan and Rodrigues* that examines the role of coronary vascular lipoprotein lipase in fatty acid delivery to the heart, and how an increase in its activity is a prelude for the cardiovascular complications seen in diabetes. The chapter of *Glatz and Liuken* then describes how fatty acids are transported into the myocardium, and the pivotal role of CD36 in the overall regulation of myocardial fatty acid uptake and utilization. *Lopaschuk* reviews the metabolic alterations that occur in heart failure associated

with obesity and diabetes, and the molecular mechanisms responsible for these changes, while *Vega, Leone, and Kelly* summarize our current understanding of the perturbations in the gene regulatory pathways that occur during the development of heart failure. This is followed by a chapter from *Aasum* that focuses on our current understanding of how myocardial substrate supply and/or utilization contribute to altered cardiac efficiency. The chapter of *Sack* discusses the key role of acetylation and its regulatory control is explored in the context of the control of mitochondrial integrity and metabolic functioning.

The second part explores alterations in cardiac energy metabolism that can occur in heart disease. *Sharma and McNeill* summarize the results of studies investigating how β -adrenergic signaling controls cardiac metabolism, and the significance of these mechanisms in diabetes. *Lygate and Neubauer* describe the complexities of changes in energy metabolism in heart failure, and the central role that alterations in creatine kinase have on these processes. *Kolwicz and Tian* focus on advances in the understanding of cardiac metabolic plasticity in pathological cardiac hypertrophy and heart failure as well as therapeutic strategies based on these observations. The key role of mitochondrial dysfunction with respect to energy production due to ischemia reperfusion injury is discussed by *Dhalla and his coworkers* and the involvement of oxidative stress and intracellular Ca^{2+} -overload in these processes has been emphasized. *Byrne, Sung, and Dyck* review the role of AMPK in the control of cardiomyocyte growth and discuss the potential benefits and pitfalls that may accompany the approach of pharmacologically activating AMPK to control the pathogenesis of cardiac hypertrophy. *Ussher* focuses on the potential role of incomplete fatty acid β -oxidation in the heart as a mediator of cardiac insulin resistance.

Finally, the third part of this book explores the exciting concept that optimizing energy metabolism may be a clinical approach to treat heart disease. *Marzilli and associates* discuss the clinical data demonstrating that inhibiting fatty acid oxidation and increasing glucose oxidation as an approach to treat ischemic heart disease. The chapter by *Gao and coworkers* reviews the existing evidence for inhibition of fatty acid oxidation to treat heart failure. Further studies are needed to confirm the potential benefit of modulating these metabolic targets as an approach to treating heart failure in clinical settings. The chapter by *Ralphe and Scholz* then examines the role of the neonatal myocyte in the heart disease, and approaches to improve myocardial preservation that is an essential part of open-heart surgery in infants and children. In the end *Portman and Olson* have presented transcriptional modulation of fatty acid oxidation as a potential therapy for heart failure.

A major contributor to our understanding of how diseases such as diabetes can impact cardiac energy metabolism is Professor John McNeill. Fittingly, this book is dedicated to Professor McNeill in order to recognize his many contributions to this important research area. Indeed, we are grateful to all contributors for providing state of the art articles and thus making this book a reality. Our thanks are also extended to both Dr. Vijayan Elimban and Ms. Eva Little at the St. Boniface Hospital Research Centre for the time and efforts which they devoted on this project. We appreciate the help of Ms. Diana Ventimiglia as well as the staff at the

Springer Media, New York in the preparation of this book. It is our sincere hope that this book will be a valuable source of information to graduate students, postdoctoral fellows, and investigators in the field of experimental cardiology as well as biochemists, physiologists, pharmacologists, cardiologists, cardiovascular surgeons, and other health professionals.

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