Dennis V. Cokkinos *Editor*

Introduction to Translational Cardiovascular Research



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Editor Dennis V. Cokkinos, MD, FESC Biomedical Research Foundation Academy of Athens Athens Greece

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All the authors dedicate this book to our families and our students. The editor (DVC) additionally dedicates it to his wife Vana, in translation

Foreword

It is with great pleasure that I write this foreword for two reasons:

First, the concept of this book emerged from two seminars held in our institution with the same title, *Introduction to Translational Cardiovascular Research*, with Professor Dennis V. Cokkinos, Director of the Heart and Vessel Department, who is also the Editor of this book as the course organizer, and Professor Evangelia Kranias, Director of Molecular Biology, Hanna Professor of Cardiology, Chair, Department of Pharmacology and Cell Biophysics, University of Cincinnati College of Medicine as co-organizer.

These courses were attended by young researchers either from a basic or a clinical background; many of them are students at or collaborating with our center.

Also, most of the instructors in this course, who have also authored the 31 chapters of the book, are either researchers or collaborators of our foundation.

Second, the Biomedical Research Foundation Academy of Athens, at its inception in 1992 and its inauguration in 2002, has been dedicated to the concept of translational research. This concept originated in the decade of 1990, and in essence, it concerns the successful implementation of laboratory findings in clinical care. When we refer to clinical care, we include the individual patient with his inalienable rights to health, quality of life, and wellbeing, but also the community and, finally, world health policies.

Although the value of basic research, which pertains to the quest of pure scientific knowledge, and clinical research, which includes mechanisms of human disease, therapeutic interventions, clinical trials, and the development of new technologies is well appreciated, there clearly exists a need for their integration, which defines translational research. This is not an easy task; meticulous planning, organizational expertise, and a generous budget allotment are essential. Our foundation strives to meet these challenges in collaboration with other institutes in Greece and abroad dedicated to these same meritorious goals.

I believe that this book, which represents a great effort by its Editor, Professor Dennis V. Cokkinos and all the participating authors, will further contribute to the awareness of the value of translational research.

I hope that it may prove successful and pursue a course productive to our application of research toward an improved quality of health services for our patients.

> Professor-Academician Gregory D. Skalkeas, MD President, Biomedical Research Foundation Academy of Athens, Athens, Greece

Preface

The term "translational research" has come to stay. It reflects today's integration of basic research ("bench") findings with the clinical practice of medicine and, in a wider scope, the application of results from the individual patient ("bedside") to entire populations for the improvement of public health.

In this book, we try to offer future researchers a stimulus in as many aspects of cardiovascular research as possible so as to promote their interest in future fields of cardiovascular disease, diagnosis, and treatment.

The idea for this book emerged from two series of seminars given at the Biomedical Research Foundation of the Academy of Athens under the title *Introduction to Translational Cardiovascular Research*.

Many presentations were added, deleted, or, more importantly, upregulated and transformed as the lessons progressed.

However, the constant "leitmotif" of the book is the interaction of basic and applied knowledge.

Another aspect that is constantly stressed by the editor by many crossreferrals is that the various processes described are very closely interrelated.

Inevitably, this book is incomplete and will be partially outdated by the time it appears, given the constant explosion of both knowledge and information.

As editor, I have tried to give a logical sequence to the chapters. Thus, fundamental and important aspects are discussed first: an introduction to the subject, translational research, cardiac development and regeneration, basis of cell excitability, and conduction. Next, I thought appropriate to describe the great axes such as the renin-angiotensin-aldosterone system, the beta adrenergic receptors, and the hypothalamic-pituitary-adrenal axis.

After this, the ubiquitous and constantly enlarging subject of genetic polymorphisms is discussed both generally and specifically as regards the vascular endothelium, which involves so many mechanisms regulating cardiac and vascular structure and function. MicroRNAs are another constantly expanding subject; they are practically involved in all processes affecting the cardiovascular system as well as the organism as a whole.

The next unit that is discussed concerns fundamental processes such as cardiac hypertrophy, calcium cycling, inflammation, stress proteins and the adaptive response, cell death, repair of the infarcted myocardium, and myocardial remodeling, together with the arrhythmic potential of the heart. Animal models of cardiovascular disease are subsequently described together with the aspects of the assessment of cardiac function and imaging in vitro in animals and in man. Next are discussed two currently widely studied entities in which novel, both basic and clinical knowledge is constantly emerging: the cardiomyopathies and the cardiorenal syndrome.

The book finishes with therapeutic aspects strongly pertaining to the interaction of basic and clinical research: pre-, peri-, and postconditioning and gene and cell therapy.

As a final chapter, an article on the translational application of the results of the continuously expanding heart failure trials is included.

Inevitably, there is considerable overlap of the data presented in the various chapters. However, all the processes described have many common pathways and mechanisms of action.

When starting this endeavor, I was asked by Springer to whom this book was addressed. The answer came gradually through the comments of the students attending these seminars and their numerous enlivening questions. Thus, it can be proposed that this book pertains to young physicians, nurses, and other scientists engaged in the clinical cardiovascular field who want to add a research-oriented dimension to their efforts toward a better understanding and practice of medicine. It also aims to attract young basic researchers who want to develop a better comprehension of the organism as a whole, man or animal, which they are investigating.

I want to express my gratitude to all the authors of this book, who also are significant contributors in their respective fields. First as teachers, they gave their best efforts to educate the young translational investigators of the future. We should not forget the wise aphorism of Henry Brooks Adams:

A teacher affects eternity. He can never tell where his influence stops.

The same teachers, often with the aid of other colleagues, expressed their thoughts in print with great diligence. Our collaboration has always been friendly, punctual, and rewarding. They are the protagonists of this book, together with our students, whose interest and curiosity prompted many outstanding considerations included in this volume.

If the current endeavor proves successful, an ongoing process of evolution will hopefully commence.

Acknowledgments and thanks are due to many:

I am indebted to all the contributors: teachers, authors, and students. Foremost, Professor Evangelia Kranias is my cochair of the course from which this book originated. She added her prestige, suggestions, and insight.

Theodora Tzanavari is a constant asset as course organizer. Additionally, her help in editing manuscripts and the work in print is invaluable.

My secretary Athinais Danou generously contributed her outstanding talents and painstaking conscientiousness throughout this effort. Tonia Kyriakoulakou and Konstantinia Karpouzi also contributed their valuable secretarial aid.

The Biomedical Research Foundation Academy of Athens, a center of international excellence, is strongly represented in this book both by faculty and students. This foundation, which, in essence, made this book possible by its organizational help, practical support, and creative environment, is the result of the vision and inspired leadership of Professor Academician Gregory D. Skalkeas, my mentor of 45 years, who contributes a foreword to the volume.

The initiation of this series and the support of the efforts toward the production of the book would not be possible without the generous financial support of the Onassis Foundation and its President Mr. Anthony Papadimitriou, a true and long-standing friend. Mr. Grant Weston of the Springer Publishing Company strongly encouraged me in planning, editing, and finishing this book.

Ms. Govindan Meena has been an outstanding project manager.

The Editor joins the faculty in dedicating this book to our families and to our students over the years, especially those who attended these seminars; they are all a constant inspiration.

I personally dedicate it additionally as a translation of my lifelong gratitude to my wife Vana.

I have tried to give due thanks to all my co-contributors for the possible success of this book. If this does not materialize as hoped, the responsibility rests solely with the Editor.

> Dennis V. Cokkinos, MD, FESC Professor Emeritus University of Athens, Honorary Director Onassis Cardiac Surgery Center, Heart and Vessel Department, Biomedical Research Foundation of the Academy of Athens, Athens, Greece

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