Klaus-Dieter Schlüter *Editor*

Cardiomyocytes – Active Players in Cardiac Disease

Springer

Cardiomyocytes – Active Players in Cardiac Disease

Klaus-Dieter Schlüter
Editor

Cardiomyocytes – Active Players in Cardiac Disease

Springer

Editor
Klaus-Dieter Schlüter
Institute of Physiology
Justus-Liebig-Universität Giessen
Giessen
Germany

ISBN 978-3-319-31249-1 ISBN 978-3-319-31251-4 (eBook)
DOI 10.1007/978-3-319-31251-4

Library of Congress Control Number: 2016943117

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG Switzerland

Preface

In this book, scientists well established in the field describe the fascinating biology of cardiomyocytes, cells that keep us alive and that are perfectly adapted to perform regulatory contractile activity throughout every minute, every hour, every day, and year by year. Failure of regular heartbeat will necessarily lead to death of the whole organism. Therefore, the understanding of the biology of cardiomyocytes, that means the understanding of their capacity to adapt to different workload, their ability to use different substrates to generate energy that allows them to keep contracting, their ability to restructure their contractile elements, and their ability to withstand various stressors is the basis to improve our clinical options with respect to heart failure, one of the biggest challenges in medicine. That is why this book is intended to give an overview about the current understanding of the biology of cardiomyocytes.

Getting the possibility to isolate and culture terminal-differentiated cardiomyocytes is and was the key step to learn and study precisely the biology of cardiomyocytes in its pure sense. Chapter 1 will briefly review the process that has been developed to reach this aim and gives a methodological overview how we can analyze basal functions of these cells. Chapter 2 recapitulates the ontogenetic history of cardiomyocytes and explains their heterogeneity in the heart and the specific function of cardiomyocytes in the adult heart. Chapter 3 introduces the principles of electromechanical coupling with a strong focus on the unique electrophysiological properties of these cells. In Chap. 4, we will learn how these cells can use different energy sources and how they adapt these mechanisms due to alternations in workload and substrate availability. In Chap. 5, it is outlined in great detail how cardiac function can be adapted to acute changes in workload. Cellular molecules are identified that are targeted by neurohumoral factors to respond to increased workload. Mechanisms different from acute adaptations are required if workload remains high. The initiation of such processes, summarized by the term cardiac hypertrophy, will be described in Chap. 6. Proteins have a distinct halftime. Therefore, cardiomyocytes must be able to degrade their proteins and if required must regulate the function of their protein degradation machinery. This is certainly another prerequisite for cardiac adaptation and remodeling. Chapter 7 will introduce all aspects of protein degradation. Cardiomyocytes normally require oxygen to generate energy. However, they have established strategies that allow them to withstand at least small periods of ischemia. How cardiomyocytes react to ischemia and how they can deal

with this challenge are discussed in Chap. 8. Even cardiomyocytes die. They have established several pathways to induce apoptosis, necrosis, and necroptosis to avoid further damage to their neighboring cells. Such mechanisms are explained in Chap. 9. Finally, although oxygen is required for cardiac function, it is also toxic. Cardiomyocytes must develop strategies to protect themselves against oxidative stress but at the same time, they have learned to use such molecules as signals. These mechanisms will be summarized in Chap. 10.

I have to thank all the authors for their contribution to this book. Without their input, this description about the biology of cardiomyocytes would be incomplete. Many thanks to all of them! I also have to thank the editors who gave me the motivation to start this project. I have learned a lot during the process of editing this book about these fascinating cells. I hope that the reader will share our enthusiasm about this interesting field of biology.

Giessen, Germany K.-D. Schlüter

Contents

Contributors

Oliver Drews Division of Cardiovascular Physiology, Institute of Physiology and Pathophysiology, Heidelberg University, Heidelberg, Germany

Gerhild Euler Institute of Physiology, Justus Liebig University, Giessen, Germany

Jacqueline Heger Institute of Physiology, Justus-Liebig-Universität Gießen, Giessen, Germany

Jens Kockskämper Institut für Pharmakologie und Klinische Pharmazie, Philipps-Universität Marburg, Marburg, Germany

Fabio Di Lisa Department of Biomedical Science, University of Padova, Padova, Italy

Bernd Niemann Klinik für Herz-, Kinderherz und Gefäßchirurgie Justus-Liebig-Universität Gießen, Giessen, Germany

Susanne Rohrbach Institute of Physiology, Justus-Liebig-Universität Gießen, Giessen, Germany

Klaus-Dieter Schlüter Institute of Physiology, Justus-Liebig-Universität Gießen, Giessen, Germany

Rolf Schreckenberg Institute of Physiology, Justus-Liebig-Universität Gießen, Giessen, Germany

Rainer Schulz Institute of Physiology, Justus-Liebig-Universität Gießen, Giessen, Germany

Marten Szibor Institute of Biotechnology, University of Helsinki, Helsingin Yliopisto, Finland

Abbreviations

AAV	Adeno-associated virus
ACE	Angiotensin converting enzyme
ACh	Acetylcholine
ADP	Adenosine diphosphate
ADR	Adrenaline
AIF	Apoptosis-inducing factor
Alk	Activin receptor-like kinase
AP	Action potential
AP-1	Activator protein-1
ATP	Adenosine triphosphate
AM	Acetoxymethyl
AMP	Adenosine monophosphate
AMPK	AMP kinase
Ang	Angiotensin
ANP	Atrial natriuretic peptide
ANT	Adeninin nucleotide translocase
AT	Angiotensin receptor
Atg	Autophagy related
AV	Atrioventricular (= node of Aschoff and Tawara)
BAT	Baroreceptor activation therapy
BCAA	Branched-chain amino acids
BCAT	Branched-chain aminotransferase
BCKA	Branched-chain keto acids
BCKAD	Branched-chain keto acid dehydrogenase complex
BDM	Butanedione monoxime
bHLH	Basic helix-loop-helix
BMP	Bone morphogenic protein
BNP	Brain natriuretic peptide
CaMK	Calcium-calmodulin-dependent protein kinase
cAMP	Cyclic adenosine monophosphate
cGMP	Cyclic guanosine monophosphate
CASA	Chaperone-assisted selective autophagy
CAT	Carnitine acylcarnitine translocase
CaT	Calcium transients

CD	Cluster of differentiation
CHD	Congenital heart disease
CHF	Chronic heart failure
CICR	Calcium-induced calcium release
CK	Creatine kinase
CNC	Cardiac neural crest
CNCC	Cardiac neural crest-derived cells
CPT	Carnitine palmitoyltransferase
CT	Central
CTP	Carnitine Palmitoyltransferase
CVLM	Caudal ventrolateral medulla
DAD	Delayed afterdepolarization
DAG	Diacylglycerol
DGS/VCFS	DiGeorge or velo-cardio-facial syndrome
DISC	Death-induced signalling complex
Drp	Dynamin-related protein
EC	Excitation-contraction
EndoG	Endonuclease G
EOMES	Eomesodermin
EPAC	Exchange protein directly activated by cAMP
EPDC	Epicardium-derived cells
EMT	Epithelial to mesenchymal transcription
ER	Endoplasmatic reticulum
ERK	Extracellular responsive kinase
ET	Endothelin
ETC	Electron transport chain
ETF:Q	Electron transfer flavoproptein-ubiquinone
FAT	Fatty acid translocase
FABP	Fatty acid-binding protein
FACS	Fatty acetyl-CoA synthase
FAO	Fatty acid oxidation
FATP	Fatty acid transport proteins
FFA	Free fatty acids
FGF	Fibroblast growth factor
FHC	Familiar hypertrophic cardiomyopathy
FHF	First heart field
FKBP	FK506-binding protein
FoxH	Forkhead box H
FWHA	Full width at half amplitude
GDP	Guanosine diphosphate
GFP	Green fluorescence protein
GPCR	G-protein-coupled receptors
Gpx	Glutathione peroxidase
GRK	G-protein-coupled receptor kinase
GTP	Guanosine triphosphate

HCN	Hyperpolarization-activated and cyclic-nucleotide-regulated channel
HDAC	Histone-deacetylase
HIF	Hypoxia-inducible factor
HT	Histamine
HtrA	High temperature requirement protein A
Hz	Hertz
IAP	Intracellular caspase inhibitor
IGF	Insulin-like growth factor
IHD	Ischemic heart disease
IMS	Intermembrane space
IP	Inositol phosphate
I/R	Ischemia/reperfusion
Isl	Islet
JAK	Janus kinase
JNK	c-Jun N-terminal Kinase
K2P	K-2-Pores
Kir	K-inward rectifying
LAMP	Lyosome-associated membrane protein
LC	Light chain
LCFA	Long-chain fatty acid
LDH	Lactate dehydrogenase
lncRNA	Long non-coding RNA
LO	Lipoxygenase
LTCC	L-type calcium channels
LVAD	Left ventricular assist device
LVEDP	Left ventricular end-diastolic pressure
MAP	Mitogen-activated protein
MCU	Mitochondrial uniporter
Mef	Myocyte-specific enhancer factor
MEK	Mitogen-activated protein kinase kinase
Mesp	Mesoderm posterior
MHC	Myosin heavy chain
MI	Myocardial Infarction
Mito-Q	Mito-quninone
MPTP	Mitochondrial permeability transition pore
MOMP	Mitochondrial outer membrane permeabilisation
mRNA	Messenger RNA
miRNA	MicroRNA
mTOR	Mammalian target of rapamycin
MuRF	Muscle ring finger
MyBP-C	Myosin-binding protein-C
NCX	Na-Ca-exchanger
Nec	Necrostatin
NFAT	Nuclear factor of activated T cells
NHE	Na-H-exchanger

NKA	Na-K-ATPase
NO	Nitric oxide
NOR	Noradrenaline
NOS	Nitric oxide synthase
NOX	NADPH oxidase
NYHA	New York Heart Association
NTS	Nucleus tractus solitarii
OxPhos	Oxidative phosphorylation
PAH	Pulmonary arterial hypertension
PCI	Percutaneous coronary intervention
PE	Phosphatidylethanolamine
PLC	Phospholipase C
PCr	Phosphocreatine
PDE	Phosphodiesterase
PDGF	Platelet-derived growth factor
PDH	Pyruvate dehydrogenase complex
PDP	Pyruvate dehydrogenase complex kinase
PDP	Pyruvate dyhdrogenase phosphatase
PFK	Phosphofructokinase
PGC	PPAR-gamma-coactivator
PI3K	Phophoinositide 3 kinase
PLB	Phospholamban
POLG	Polymerase gamma
PKA	Protein kinase A
PKC	Protein kinase C
PP	Protein phosphatase
PPP	Pentose phosphate pathway
PPAR	Peroxisome-proliferator-activated receptor
PRC	Polycomb-repressive complex
PTM	Post-translational modification
RAAS	Renin-angiotensin-aldosterone-system
RIPK	Receptor interacting protein kinase
RISC	RNA-induced silencing complex
RIS	Reactive inflammatory species
RISK	Reperfusion injury salvage kinase
ROS	Reactive oxygen species
rhNRG	Recombinant human neuregulin
RNS	Reactive nitrogen species
RyR	Ryanodine receptor
RVH	Right ventricular hypertrophy
RVLM	Rostral ventrolateral medulla
SA	Sinoatrial
SERCA	SR-calcium-ATPase
SHF	Second heart field
SK	Small conductance