Klaus-Dieter Schlüter Editor

Cardiomyocytes – Active Players in Cardiac Disease



Cardiomyocytes – Active Players in Cardiac Disease

Klaus-Dieter Schlüter Editor

Cardiomyocytes – Active Players in Cardiac Disease



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

© Springer International Publishing Switzerland 2016

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made.

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

| Part | I Cardiomyocytes: Function and Regeneration | |
|------|---|-----|
| 1 | Ways to Study the Biology of Cardiomyocytes | . 3 |
| 2 | Cardiomyocytes: Function and Regeneration | 25 |
| 3 | Excitation–Contraction Coupling of Cardiomyocytes | 67 |
| 4 | Cardiac Metabolism and Energetic Control | 97 |
| 5 | Endogenous Mechanisms for Regulating Myocardial Contractility Rolf Schreckenberg | 135 |
| Part | II Cardiomyocytes in Ageing, Disease, and Protection | |
| 6 | Growth Regulation of Cardiomyocytes: Control of Cell Size and Its Role in Cardiac Hypertrophy Klaus-Dieter Schlüter | 167 |
| 7 | Protein Degradation in Cardiomyocytes: Target Proteins and Clinical Consequences Oliver Drews | 191 |
| 8 | Ischemia and Reperfusion | 223 |
| 9 | Mechanisms of Cardiac Cell Death | 247 |
| 10 | Oxidative Stress and Nitrosative Stress Rainer Schulz and Fabio Di Lisa | 267 |

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 | Chapter of differentiation |
|------------|---|
| 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 GPK | Glutathione peroxidase |
| GRK | G-protein-coupled receptor kinase |
| GTP | Guanosine triphosphate |

| HCNHyperpolarization-activated and cyclic-nucleotide-regulated channelHDACHistone-deacetylaseHIFHypoxia-inducible factorHTHistamineHtrAHigh temperature requirement protein AHzHertzIAPIntracellular caspase inhibitorIGFInsulin-like growth factorHIDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLCFALong-chain fatty acidLDHLactate dehydrogenaseInCRNALong-chain fatty acidLDHLactate dehydrogenaseINCLipoxygenaseLVEDPLeft ventricular assist deviceLVEDPLeft ventricular assist deviceLVEDPLeft ventricular assist deviceLVEDPLeft ventricular assist deviceMAPMitogen-activated protein kinase kinaseMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-dondrial outer membrane permeabilisationMRNAMessenger RNAMEXMessenger RNAMEXMito-dondrial outer membrane permeabilisation |
|---|
| HIFHypoxia-inducible factorHTHistamineHtrAHigh temperature requirement protein AHzHertzIAPIntracellular caspase inhibitorIGFInsulin-like growth factorIHDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateI/RIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular assist deviceLVEDPLeft ventricular assist deviceMAPMitogen-activated proteinMCUMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyocyte-specific enhancer factorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMitochondrial outer membrane permeabilisation poreMOMPMitochondrial outer membrane permeabilisation |
| HTHistamineHtrAHigh temperature requirement protein AHzHertzIAPIntracellular caspase inhibitorIGFInsulin-like growth factorIHDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateI/RIschemia/reperfusionIslIsletJAKKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVADLeft ventricular assist deviceMAPMitogen-activated proteinMCUMitogen-activated protein kinase kinaseMAPMoyoeyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMitochondrial outer membrane permeabilisation poreMOMPMitochondrial outer membrane permeabilisation |
| HtrAHigh temperature requirement protein AHzHertzIAPIntracellular caspase inhibitorIGFInsulin-like growth factorIHDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateI/RIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLVADLeft ventricular assist deviceLVADLeft ventricular assist deviceLVADLeft ventricular end-diastolic pressureMAPMitogen-activated protein kinase kinaseMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocrdial InfarctionMito-QMitochondrial outer membrane permeabilisation poreMOMPMitochondrial outer membrane permeabilisation |
| HzFertzIAPIntracellular caspase inhibitorIGFInsulin-like growth factorIHDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateI/RIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVEDPLeft ventricular assist deviceLVEDPLeft ventricular assist deviceMAPMitogen-activated protein factorMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMICQMitochondrial outer membrane permeabilisation poreMOMPMitochondrial outer membrane permeabilisationmRNAMesenger RNA |
| IAPIntracellular caspase inhibitorIGFInsulin-like growth factorIHDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateI/RIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseInCCLipoxygenaseLTCCLipoxygenaseLTCCLeft ventricular assist deviceLVEDPLeft ventricular assist deviceLVEDPLeft ventricular assist deviceMAPMitogen-activated protein kinase kinaseMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMICMyosin heavy chainMIMyocardial InfarctionMIPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| IGFInsulin-like growth factorIHDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateIPInositol phosphateIRIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular assist deviceLVEDPLeft ventricular opticin kinase kinaseMAPMitogen-activated protein kinase kinaseMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMITMyocardial InfarctionMITMyocardial InfarctionMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| IHDIschemic heart diseaseIMSIntermembrane spaceIPInositol phosphateIPInositol phosphateI/RIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| IMSIntermembrane spaceIPInositol phosphateIPInositol phosphateIRIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular assist deviceLVEDPLeft ventricular assist deviceMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| IPInositol phosphateI/RIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated protein kinaseMEKMitogen-activated protein kinaseMEKMitogen-activated protein kinaseMBFMyocyte-specific enhancer factorMILMyocardial InfarctionMIACMyosin heavy chainMIMyocardial InfarctionMIACMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| I/RIschemia/reperfusionIslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated protein hanseMEKMitogen-activated protein kinase kinaseMEKMitogen-activated protein kinase kinaseMFMyocyte-specific enhancer factorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| IslIsletJAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular assist deviceMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| JAKJanus kinaseJNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaseIncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular assist deviceMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| JNKc-Jun N-terminal KinaseK2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| K2PK-2-PoresKirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| KirK-inward rectifyingLAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LAMPLyosome-associated membrane proteinLCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LCLight chainLCFALong-chain fatty acidLDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMICMyocardial InfarctionMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LCFALong-chain fatty acidLDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMICMyosin heavy chainMIMyocardial InfarctionMito-QMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LDHLactate dehydrogenaselncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMEKMitogen-activated protein kinase kinaseMEKMitogen-activated protein kinase kinaseMEKMitogen-activated protein kinase kinaseMEKMitogen-activated protein kinase kinaseMFDMesoderm posteriorMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| IncRNALong non-coding RNALOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LOLipoxygenaseLTCCL-type calcium channelsLVADLeft ventricular assist deviceLVADLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LTCCL-type calcium channelsLVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LVADLeft ventricular assist deviceLVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| LVEDPLeft ventricular end-diastolic pressureMAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MAPMitogen-activated proteinMCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MCUMitochondrial uniporterMefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MefMyocyte-specific enhancer factorMEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MEKMitogen-activated protein kinase kinaseMespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MespMesoderm posteriorMHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MHCMyosin heavy chainMIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MIMyocardial InfarctionMito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| Mito-QMito-quninoneMPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MPTPMitochondrial permeability transition poreMOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| MOMPMitochondrial outer membrane permeabilisationmRNAMessenger RNA |
| 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 |
| РКА | Protein kinase A |
| РКС | 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 |
| | |