



Universiteit
Leiden
The Netherlands

Quantifying functional phenotypes in human pluripotent stem cell derived cardiomyocytes for disease modelling and drug discovery

Meer, B.J. van

Citation

Meer, B. J. van. (2020, November 3). *Quantifying functional phenotypes in human pluripotent stem cell derived cardiomyocytes for disease modelling and drug discovery*. Retrieved from <https://hdl.handle.net/1887/138008>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/138008>

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/138008> holds various files of this Leiden University dissertation.

Author: Meer, B.J. van

Title: Quantifying functional phenotypes in human pluripotent stem cell derived cardiomyocytes for disease modelling and drug discovery

Issue date: 2020-11-03

Quantifying functional phenotypes in human pluripotent stem cell derived cardiomyocytes for disease modelling and drug discovery

Berend van Meer

Colophon

Quantifying functional phenotypes in human pluripotent stem cell derived cardiomyocytes for disease modelling and drug discovery

Berend Jan van Meer
Thesis Leiden University Medical Center

Cover illustration & design by Mariëtte Kooren
ISBN 978-94-6423-022-2

Copyright: © Berend van Meer, Haarlem, the Netherlands
All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means without permission of the author, or, when applicable, of the publishers of the scientific papers.

Quantifying functional phenotypes in human pluripotent stem cell derived cardiomyocytes for disease modelling and drug discovery

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof.mr. C.J.J.M. Stolker,
volgens besluit van het College voor Promoties
te verdedigen op dinsdag 3 november 2020
klokke 16.15 uur

door

Berend Jan van Meer
geboren te Bloemendaal
in 1988

Promotor	Prof. dr. C.L. Mummery
Co-promotor	Dr. L.G.J. Tertoolen
Promotiecommissie	Prof. dr. M.J.T.H. Goumans Prof. dr. D.E. Atsma Prof. dr. A.P. IJzerman Prof. dr. ir. R. Dekker Prof. dr. J. Bakkers

This research was conducted at the Department of Embryology & Anatomy of the Leiden University Medical Center, the Netherlands. It was supported by research grants from the European Research Council, the National Centre for the Replacement, Refinement and Reduction of Animals in Research and the Dutch Research Council.

Publication of this thesis was financially supported by Stichting Proefdiervrij, the Dutch Heart Foundation and the Willy van Heumenfonds.

Aan mijn ouders,
voor oneindig veel vertrouwen

Table of contents

1	General introduction	8
2	Measuring physiological responses of human pluripotent stem cell derived cardiomyocytes to drugs and disease	20
3	MUSCLEMOTION: a versatile open software tool to quantify cardiomyocyte and cardiac muscle contraction <i>in vitro</i> and <i>in vivo</i>	40
4	Quantification of muscle contraction <i>in vitro</i> and <i>in vivo</i> using MUSCLEMOTION software: from stem cell-derived cardiomyocytes to zebrafish and human hearts	74
5	Simultaneous measurement of excitation-contraction coupling parameters identifies mechanisms underlying contractile responses of hiPSC-derived cardiomyocytes	104
6	Blinded, multi-centre evaluation of drug-induced changes in contractility using human induced pluripotent stem cell-derived cardiomyocytes	138
7	Cytostretch, an Organ-on-Chip platform	200
8	Small molecule absorption by PDMS in the context of drug response bioassays	224
9	General discussion and future perspectives	240
	Summary	250
	Nederlandse samenvatting	254
	Curriculum vitae	258
	List of publications	260
	Dankwoord	262