

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/39392> holds various files of this Leiden University dissertation

**Author:** Engels, Marc Christian

**Title:** Cellular modifications and interventions for the damaged heart

**Issue Date:** 2016-05-11

# **Cellular Modifications and Interventions for the Damaged Heart**

**Marc C. Engels**

## Colophon

### **Cellular Modifications and Interventions for the Damaged Heart**

Marc C. Engels

The studies described in this thesis were performed at the Laboratory of Experimental Cardiology of the Department of Cardiology of the Leiden University Medical Center, Leiden, the Netherlands, and the Cardiovascular Research Center of the Massachusetts General Hospital, Boston, MA, U.S.A.

Copyright © 2016 Marc C. Engels

All rights reserved. No parts of this thesis may be reproduced, stored in a retrieval system of any nature or transmitted in any form or by any means, photocopied, recorded or otherwise, without prior written permission of the author, or when appropriate, the publishers of the papers.

**ISBN:** 978-90-9029675-3

**Support:** The research described in this thesis was supported by the Netherlands Organization for Scientific Research (NWO) through a Mosaic grant (017.007.064).

**Cover:** Deirdre Waski

**Lay-out and printed by:** Gildeprint, Enschede, the Netherlands

# **Cellular Modifications and Interventions for the Damaged Heart**

## **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 woensdag 11 mei 2016  
klokke 16:15 uur

door

**Marc Christian Engels**  
geboren te Willemstad, Curaçao  
in 1984

**Promotor:**

Prof. dr. M.J. Schalijs

**Co-Promotores:**

Dr. D.A. Pijnappels

Dr. A.A.F. de Vries

**Promotiecommissie:**

Prof. dr. D.E. Atsma

Prof. dr. V.M. Christoffels (Universiteit van Amsterdam)

Dr. S.M. Wu (Stanford University, Stanford, CA, U.S.A.)

Prof. Dr. K. Zeppenfeld

Stay hungry. Stay foolish.

-Steve Jobs (excerpt from Stanford commencement address, 12 June 2005)

*In loving memory of my grandparents*

*To my parents*

*For Becca*



## Contents

<b>Chapter 1</b>	<b>General introduction and outline of thesis</b>	<b>9</b>
<b>Chapter 2</b>	<b>Reprogramming of mouse, rat, pig, and human fibroblasts into iPS cells</b> Rajarajan K, Engels MC, Wu SM Current Protocols in Molecular Biology 2012;Chapter 23:Unit 23.15	<b>25</b>
<b>Chapter 3</b>	<b>Insulin-like growth factor promotes cardiac lineage induction in vitro by selective expansion of early mesoderm</b> Engels MC, Rajarajan K, Feistritz R, Sharma A, Nielsen UB, Schali J MJ, de Vries AA, Pijnappels DA, Wu SM Stem Cells 2014;32:1493-1502	<b>67</b>
<b>Chapter 4</b>	<b>Forced fusion of human ventricular scar cells with cardiomyocytes suppresses arrhythmogenicity in a co-culture model</b> Engels MC, Askar SF, Jangsangthong W, Bingen BO, Feola I, Liu J, Majumder R, Versteegh MI, Braun J, Klautz RJ, Ypey DL, De Vries AA, Pijnappels DA Cardiovascular Research 2015;107:601-612	<b>93</b>
<b>Chapter 5</b>	<b>Islands of spatially discordant APD alternans underlie arrhythmogenesis by promoting electrotonic dyssynchrony in models of fibrotic rat ventricular myocardium</b> Engels MC, Majumder R, de Vries AA, Panfilov AV, Pijnappels DA Scientific Reports 2016;6:24334	<b>131</b>
<b>Chapter 6</b>	<b>Light-induced termination of spiral wave arrhythmias by optogenetic engineering of atrial cardiomyocytes</b> Bingen BO, Engels MC, Jangsangthong W, Neshati Z, Feola I, Ypey DL, Askar SF, Panfilov AV, Pijnappels DA, de Vries AA Cardiovascular Research 2014;104:194-205	<b>169</b>
<b>Chapter 7</b>	<b>Summary, conclusions and future perspectives</b>	<b>197</b>
	<b>Nederlandse samenvatting</b>	<b>205</b>
	<b>List of Publications</b>	<b>211</b>
	<b>Acknowledgements</b>	<b>213</b>
	<b>Curriculum Vitae</b>	<b>215</b>



