

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/21063> holds various files of this Leiden University dissertation.

Author: Ewing, Mark McConnell

Title: Post-interventional atherosclerotic vascular remodeling : preclinical investigation into immune-modulatory therapies

Issue Date: 2013-05-23

Post-interventional atherosclerotic vascular remodeling

Preclinical investigation into
immune-modulatory therapies

Mark M. Ewing

Post-interventional atherosclerotic vascular remodeling

Preclinical investigation into
immune-modulatory therapies

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van de Rector Magnificus prof. mr. C.J.J.M. Stolker,
volgens besluit van het College voor Promoties
te verdedigen op donderdag 23 mei 2013
klokke 15.00 uur

door

Mark McConnell Ewing

geboren te Alkmaar
in 1986

Promotiecommissie

Promotor:	Prof. dr. P.H.A. Quax
Co-promotor:	Prof. dr. J.W. Jukema
Overige leden:	Prof. dr. R.E. Toes Prof. dr. J. Hamming Prof. dr. P.J. van den Elsen Prof. dr. J. Kuiper (LACDR, Leiden University)

The research described in this thesis was performed the departments of Surgery and Cardiology in the Leiden University Medical Center, Leiden, The Netherlands.

Het verschijnen van dit proefschrift werd mede mogelijk gemaakt door steun van de Nederlandse Hartstichting.

Financial support for the printing of this thesis was provided by Boehringer Ingelheim BV, Boston Scientific, ChipSoft, Daiichi Sankyo Nederland BV, Diabetes Fonds, J.E. Jurriaanse Stichting, familie Van Mourik, MSD Nederland BV, Roche Nederland BV and Servier Nederland Farma BV.

Happiness lies in the joy of achievement and the thrill of creative effort.

Franklin D. Roosevelt
1882-1945

Aan mijn ouders & Hinka

Cover design: M.M. Ewing
Inspired by the London Underground map and reproduced with the kind permission of Transport for London.

Printing: Wöhrmann Print Service

ISBN: 978-94-6203-331-3

Mark M. Ewing
Post-interventional atherosclerotic vascular remodeling: preclinical investigation into immune-modulatory therapies.

Proefschrift Leiden
Met literatuur opgave en Nederlandse samenvatting.

© 2013 M.M. Ewing
No parts of this thesis may be reproduced or transmitted in any form or by any means without prior permission of the author.

Table of contents

		Page
		11
Chapter 1	General introduction	11
Chapter 2	Potential biomarkers for accelerated atherosclerosis and other post-interventional remodeling <i>Biomark Med.</i> 2012;6:53-66	39
Chapter 3	Small animal models to study restenosis and effects of (local) drug therapy <i>Coronary stent restenosis</i> , Editor: IC Tintoiu. Bucharest: The Publishing House of the Romanian Academy. 2011	61
Part I Annexin A5 in accelerated atherogenesis		
Chapter 4	Annexin A5 therapy attenuates vascular inflammation and remodeling and improves endothelial function in mice <i>Arterioscler Thromb Vasc Biol.</i> 2011;31:95-101	83
Chapter 5	Annexin A5 prevents post-interventional accelerated atherosclerosis development in a dose-dependent fashion <i>Atherosclerosis</i> 2012;221:333-340	107
Part II Innate and adaptive immunity in vascular remodeling		
Chapter 6	Optimizing natural occurring IgM antibodies for therapeutic use: inflammatory vascular disease treatment with anti-phosphorylcholine IgG <i>Submitted for publication</i>	127
Chapter 7	Blocking toll-like receptors 7 and 9 reduces postinterventional remodeling via reduced macrophage activation, foam cell formation, and migration <i>Arterioscler Thromb Vasc Biol.</i> 2012;32:e72-80	161
Chapter 8	T-cell co-stimulation by CD28-CD80/86 and its negative regulator CTLA-4 strongly influence accelerated atherosclerosis development <i>Int J Cardiol.</i> 2013; <i>In press</i>	189
Part III PCAF in post-interventional vascular remodeling		
Chapter 9	Genetic variation in PCAF, a key mediator in epigenetics, is associated with reduced vascular morbidity and mortality: evidence for a new concept from three independent	219

	Page
prospective studies <i>Heart.</i> 2011;97:143-50	
Chapter 10 The epigenetic factor PCAF regulates vascular inflammation and is essential for accelerated atherosclerosis development. <i>Submitted for publication</i>	237
Chapter 11 The lysine acetyltransferase PCAF is a key regulator of arteriogenesis. <i>Submitted for publication</i>	259
Chapter 12 Summary and general discussion	285
Nederlandse samenvatting	292
List of publications	299
Curriculum Vitae	302

