

Cover Page



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**Author:** Ewing, Mark McConnell

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

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## List of publications

### Book chapters

1. Ewing MM, Karper JC, de Vries MR, Jukema JW, Quax PHA. Small Animal Models to Study Restenosis and Effects of (Local) Drug Therapy. *Coronary stent restenosis*. Editor: IC Tintoiu. Bucharest: The Publishing House of the Romanian Academy, 2011.

### Full papers

2. Ewing MM, Karper JC, Abdul S, de Jong RCM, Peters HAB, de Vries MR, Redeker A, Kuiper J, Toes RE, Arens R, Jukema JW, Quax PHA. T-cell co-stimulation by CD28-CD80/86 and its negative regulator CTLA-4 strongly influence accelerated atherosclerosis development. *Int J Cardiol*. 2013; in press.
3. Karper JC, Ewing MM, Habets KLL, de Vries MR, Peters HAB, van Oeveren-Rietdijk AM, de Boer HC, Hamming JF, Kuiper J, Kandimalla ER, La Monica N, Jukema JW, Quax PHA. Blocking toll-like receptors 7 and 9 reduces postinterventional remodeling via reduced macrophage activation, foam cell formation, and migration. *Arterioscler Thromb Vasc Biol*. 2012;32:e72-80.
4. Ewing MM, Karper JC, Sampietro ML, de Vries MR, Pettersson K, Jukema JW, Quax PHA. Annexin A5 prevents post-interventional accelerated atherosclerosis development in a dose-dependent fashion. *Atherosclerosis* 2012;221:333-340.
5. Ewing MM, Karper JC, Jukema JW, Quax PH. Future potential biomarkers for postinterventional restenosis and accelerated atherosclerosis. *Biomark Med*. 2012;6:53-66.
6. Verschuren JJ, Sampietro ML, Pons D, Trompet S, Ewing MM, Quax PH, de Knijff P, Zwinderman AH, de Winter RJ, Tio RA, de Maat MP, Doevendans PA, Jukema JW. Matrix metalloproteinases 2 and 3 gene polymorphisms and the risk of target vessel revascularization after percutaneous coronary intervention: Is there still room for determining genetic variation of MMPs for assessment of an increased risk of restenosis? *Dis Markers*. 2010;29:265-73.
7. Pons D, Trompet S, de Craen AJ, Thijssen PE, Quax PH, de Vries MR, Wierda RJ, van den Elsen PJ, Monraats PS, Ewing MM, Heijmans BT, Slagboom PE, Zwinderman AH, Doevendans PA, Tio RA, de Winter RJ, de Maat MP, Iakoubova OA, Sattar N, Shepherd J, Westendorp RG, Jukema JW. 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 prospective studies. *Heart*. 2011;97:143-50.

8. Ewing MM, de Vries MR, Nordzell M, Pettersson K, de Boer HC, van Zonneveld AJ, Frostegård J, Jukema JW, Quax PH. Annexin A5 therapy attenuates vascular inflammation and remodeling and improves endothelial function in mice. *Arterioscler Thromb Vasc Biol.* 2011;31:95-101.
9. Bergheanu SC, Pons D, Karalis I, Ozsoy O, Verschuren JJW, Ewing MM, Quax PHA, Jukema JW. Genetic determinants of adverse outcome (restenosis, malapposition and thrombosis) after stent implantation. *Interventional Cardiology.* 2010;2:147-157.
10. Ewing MM, Karabina SAP, Nordzell M, Atout R, Sexton D, Lettesjö H, Karper JC, de Vries MR, Dahlbom I, Camber O, Frostegård J, Ninio E, Jukema JW, Pettersson K, Quax PHA. Optimizing Natural Occurring IgM Antibodies for Therapeutic Use: Inflammatory Vascular Disease Treatment with Anti-Phosphorylcholine IgG. *Submitted for publication.*
11. Ewing MM, Karper JC, Peters HAB, Bastiaansen AJNM, de Vries MR, van den Elsen PJ, Gongora C, Maurice T, Jukema JW, Quax PHA. The epigenetic factor PCAF regulates vascular inflammation and is essential for accelerated atherosclerosis development. *Submitted for publication.*
12. Bastiaansen AJ, Ewing MM, de Boer HC, van der Pouw Kraan TC, de Vries MR, Peters HAB, Arens R, Moore SM, Faber JE, Jukema JW, Hamming JF, Nossent AY, Quax PHA. The lysine acetyltransferase PCAF is a key regulator of arteriogenesis. *Submitted for publication.*
13. Karper JC, de Jager SCA, Ewing MM, de Vries MR, Bot I, van Santbrink PJ, Redeker A, Mallat Z, Binder CJ, Arens R, Jukema JW, Kuiper J, Quax PHA. The extracellular Toll Like Receptor 4 regulator RP105 (CD180) ameliorates atherosclerosis via its role on B-cells. *Submitted for publication.*
14. Karper JC, Ewing MM, de Vries MR, de Jager SCA, el Otmani H, Peters HAB, Sampietro ML, de Boer HC, van Zonneveld AJ, Kuiper J, Huizinga EG, Brondijk THC, Jukema JW, Quax PHA. TLR accessory molecule RP105 (CD180) is involved in post-interventional vascular remodeling and soluble RP105 modulates neointima formation. *Submitted for publication.*

## Abstracts

15. Ewing MM, Verschuren JJW, Sampietro ML, de Vries MR, De Knijff P, Quax PHA, Jukema JW. Annexin A5: Genotypic risk marker for clinical restenosis after percutaneous coronary intervention. *Eur Heart J.* 2010;31:803.
16. Karper JC, Ewing MM, de Vries MR, Sampietro ML, Jukema JW, Quax PHA. RP105, a Toll Like Receptor 4 (TLR4) homolog, moderates restenosis and outward remodeling. *Circulation.* 2010;122: A14280.

17. Ewing MM, Karabina SAP, Pettersson K, Atout R, de Vries Mr, Sexton D, Lettesjö H, Frostegård J, Jukema JW, Ninio E, Quax PHA. Anti-Phosphorylcholine IgG Antibodies Reduce Restenosis and Vascular Inflammation by Inhibition of the Unfolded Protein Response in a Mouse Model of Accelerated Atherosclerosis. *Circulation*. 2010;122: A14320.
18. Ewing MM, de Vries MR, Nordzell M, Jukema JW, Frostegård J, Pettersson K, Quax PHA. Annexin A5 Reduces Inflammation Mediated Vascular Remodelling and Post-interventional Atherosclerosis and Improves Vascular Function in Hypercholesterolemic Mice. *Circulation*. 2009;120:S1113.

## Curriculum vitae

Mark M. Ewing was born on June 29<sup>th</sup> 1986 in Alkmaar. He attended the *atheneum* at the Openbare Scholengemeenschap Willem Blaeu in Alkmaar, where he graduated *cum laude* in 2004. During the same year, he started his medical study at the Leiden University Medical Center (LUMC) in Leiden, The Netherlands.

During his study, he took up a position of student-assistant in teaching anatomy lessons for medical students and was involved in research into preclinical models for screening of immune system-based modulatory therapy for post-interventional vascular remodeling under the supervision of prof. dr. J.W. Jukema at the department of Cardiology at the LUMC and prof. dr. P.H.A. Quax at the Gaubius Laboratorium at TNO, Quality for Life, both in Leiden. He obtained his medical doctoral exam *cum laude* in 2008.

Thereafter, he continued his research which formed the basis of his PhD program conducted in the LUMC under prof. Jukema and prof. Quax at both the department of Cardiology and Surgery. This was funded by the European Sixth Framework program for research and technological development and the Circulating Cells project under auspices of the Center for Translation Molecular Medicine and is described in this thesis. In 2010, he won the prize for best oral presentation at the Vascular Medicine Symposium of the Rembrandt Institute for Cardiovascular Science hosted by the LUMC and Amsterdam Medical Center.

Starting October 2011, he is performing his medical rotations at the LUMC and the University of Leiden. From November 2013 onwards, he will continue his training as *Arts in Opleiding tot Specialist (AIOS)* Cardiology at the Onze Lieve Vrouwe Gasthuis (OLVG) in Amsterdam under supervision of dr. G.A. Somsen (department of Cardiology) and dr. Y.F.C. Smets (department of Internal Medicine). He lives in Amsterdam together with his partner Hinka.

