



Universiteit
Leiden
The Netherlands

Cell cycle and apoptosis genes in atherosclerosis

Boesten, Lianne Simone Mirjam

Citation

Boesten, L. S. M. (2006, March 1). *Cell cycle and apoptosis genes in atherosclerosis*. Retrieved from <https://hdl.handle.net/1887/4457>

Version: Corrected 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/1887/4457>

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



**CELL CYCLE AND APOPTOSIS GENES IN
ATHEROSCLEROSIS**

Lianne S.M. Boesten

2006

CELL CYCLE AND APOPTOSIS GENES IN ATHEROSCLEROSIS

PROEFSCHRIFT

ter verkrijging van
de graad van Doctor aan de Universiteit van Leiden,
op gezag van de Rector Magnificus Dr.D.D. Breimer,
hoogleraar in de faculteit der Wiskunde en
Natuurwetenschappen en die der Geneeskunde,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 1 maart 2006
klokke 14.15

door

Lianne Simone Mirjam Boesten

geboren te Tilburg in 1979

Promotiecommissie

Promotor: Prof. Dr. L.M. Havekes

Co-promotores: Dr. B.J.M. van Vlijmen
Dr. M.P.J. de Winther, Universiteit Maastricht

Referent: Prof. Dr. M.H. Hofker, Universiteit Maastricht

Overige leden: Prof.Dr.A. v.d. Laarse
Prof.Dr.A.C. Gittenberger-de Groot
Dr.T. Kooistra, TNO-Kwaliteit van Leven, Leiden

ISBN: 90-8559-104-X

The study described in this thesis was supported by a grant of the Netherlands Heart Foundation (NHF-2000.051). The studies were performed at the Gaubius Laboratories of TNO Quality of Life and the Leiden University Medical Center, Leiden, The Netherlands.

Financial support by the Netherlands Heart Foundation for the publication of this thesis is gratefully acknowledged.

The printing of this thesis was financially supported by the Dutch Atherosclerosis Society (DAS), TNO-Quality of Life, Leiden, The Netherlands and AstraZeneca, Sweden.

Cover: Paper spiral, photograph from Mauro Bighin, Padova, Italy

Print: Optima Grafische Communicatie B.V., Rotterdam

Let, als je naar een doel reist, goed op de weg.
De weg leert je de beste manier om er te komen
en verrijkt ons terwijl we hem bewandelen.

Paulo Coelho

Aan mijn ouders

Voor Michel

TABLE OF CONTENTS

Chapter 1 General Introduction	9
Chapter 2 Macrophage p53 controls foam cell death in atherosclerotic lesions of apolipoprotein E deficient mice	33
Chapter 3 Macrophage Retinoblastoma deficiency leads to enhanced atherosclerosis development in ApoE-deficient mice	47
Chapter 4 Mdm2 protects terminally differentiated smooth muscle cells from p53-mediated cell death with a necrotic morphotype	65
Chapter 5 Local Cre-mediated gene recombination in vascular smooth muscle cells in mice	83
Chapter 6 Tumor Necrosis Factor- α promotes atherosclerotic lesion progression in APOE*3-Leiden transgenic mice	93
Chapter 7 The dual PPAR α/γ agonist tesaglitazar reduces atherosclerosis development beyond its plasma cholesterol-lowering effects in APOE*3-Leiden transgenic mice	107
Chapter 8 General Discussion	125
Summary	141
Samenvatting	147
Curriculum Vitae	155
List of publications	156

