



Universiteit
Leiden
The Netherlands

CCR5 in multiple sclerosis : expression, regulation and modulation by statins

Kuipers, H.F.

Citation

Kuipers, H. F. (2007, March 28). *CCR5 in multiple sclerosis : expression, regulation and modulation by statins*. Retrieved from <https://hdl.handle.net/1887/11460>

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/1887/11460>

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

CCR5 in Multiple Sclerosis: Expression, Regulation, and Modulation by Statins

Hedwich F. Kuipers

CCR5 in Multiple Sclerosis: Expression, Regulation, and Modulation by Statins

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus Prof. Mr. P.F. van der Heijden,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 28 maart 2007
klokke 15:00 uur

door

Hedwich Fardau Kuipers

geboren te Leeuwarden
in 1979

Promotiecommissie

Promotor: Prof. Dr. P.J. van den Elsen

Referent: Prof. Dr. I. Bechmann
Johann Wolfgang Goethe-Universität, Frankfurt, Germany

Overige leden: Prof. Dr. F. Koning
Prof. Dr. F.H.J. Claas
Prof. Dr. P. van der Valk
VU Medisch Centrum, Amsterdam
Prof. Dr. C.D. Dijkstra
VU Medisch Centrum, Amsterdam

The research described in this thesis was performed at the Department of Immunohematology and Blood Transfusion of the Leiden University Medical Center in collaboration with the Department of Pathology of the VU University Medical Center, and was funded by the Dutch MS Research Foundation (grant MS 00-407).

ISBN: 978-90-9021648-5

© H.F. Kuipers, 2007

Niets uit deze uitgave mag worden verveelvoudigd en/of openbaar gemaakt worden zonder voorafgaande schriftelijke toestemming van de auteur. No part of this thesis may be reproduced in any form without written permission from the author.

Layout and coverdesign: H.F. Kuipers
Printed by: Ponsen & Looijen BV

Financial support for the publication of this thesis was provided by the Dutch MS Research Foundation and the Van Leersumfonds KNAW.

*"The Road goes ever on and on
Down from the door where it began.
Now far ahead the Road has gone,
And I must follow, if I can,
Pursuing it with eager feet,
Until it joins some larger way
Where many paths and errands meet.
And wither then? I cannot say."*

J.R.R. Tolkien, The Lord of the Rings

Paranimfen:

Hugo M. Nijhof

Tjadine M. Holling

Contents

1	Introduction	
	Central nervous system immunity & Immunomodulation by statins	9
2	CCR5 expression in MS	
	Enhanced expression of the chemokine receptor CCR5 in Multiple Sclerosis lesions	47
3	CCR5 transcriptional regulation	
	CC chemokine receptor 5 (CCR5) gene promoter activation by the cyclic AMP response element binding (CREB) transcription factor	69
4	Statins and CIITA	
	Statins and control of <i>MHC2TA</i> gene transcription	97
5	Statins and MHC-II / immunoregulatory molecules	
	Statins affect cell surface expression of major histocompatibility complex class II molecules by disrupting cholesterol-containing microdomains	107
6	Statins and microglia cell function	
	Simvastatin affects cell motility and actin cytoskeleton distribution of microglia	135
7	Statins and monocyte differentiation	
	Simvastatin inhibits differentiation of monocytes into immature DC and not DC maturation	159
8	General Discussion	177
9	Summary / Samenvatting	203
10	Curriculum Vitae	213
11	Publications	219

