



Universiteit
Leiden
The Netherlands

Genetics, autoantibodies and clinical features in understanding and predicting rheumatoid arthritis

Helm-van Mil, A.H.M. van der

Citation

Helm-van Mil, A. H. M. van der. (2006, October 26). *Genetics, autoantibodies and clinical features in understanding and predicting rheumatoid arthritis*. Retrieved from <https://hdl.handle.net/1887/4929>

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/1887/4929>

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

**Genetics, Autoantibodies and Clinical Features
in Understanding and Predicting
Rheumatoid Arthritis**

Annette van der Helm - van Mil



ISBN: 90-8559-193-7

De druk van dit proefschrift werd gedeeltelijk financieel ondersteund door: J.E. Jurriaanse Stichting, Reumafonds, Abbott B.V., Bristol-Myers-Squibb, Centocor B.V., MSD B.V., Pfizer B.V., Roche Nederland B.V., Servier Nederland B.V., Sanofi-Aventis, Wyeth Pharmaceuticals B.V.

**Genetics, Autoantibodies and
Clinical Features
in Understanding and Predicting
Rheumatoid Arthritis**

PROEFSCHRIFT

ter verkrijging van
de graad Doctor aan de Universiteit 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 van Promoties
te verdedigen op donderdag 26 oktober 2006
klokke 16.15 uur

door

Anna Helena Maria van der Helm - van Mil

Geboren te Delft
in 1974

PROMOTIECOMMISSIE

Promotores: Prof. Dr. T.W.J. Huizinga
Prof. Dr. F.C. Breedveld

Co-promotor: Dr. R.E.M. Toes

Referent: Prof. Dr. P.L.C.M. van Riel (Universiteit Nijmegen)

Leden: Dr. S. le Cessie
Prof. Dr. F. Koning
Prof. Dr. R.R.P. de Vries

CONTENTS

Chapter 1	General introduction	9
Part 1	Association of several genetic risk factors with RA	
Chapter 2	An independent role for protective HLA Class II alleles in rheumatoid arthritis severity and susceptibility. <i>Arthritis Rheum.</i> 2005;52(9):2637-44.	21
Chapter 3	No association between Tumor Necrosis Factor Receptor Type 2 gene polymorphism and rheumatoid arthritis severity: a comparison of the extremes of phenotypes. <i>Rheumatology (Oxford).</i> 2004;43(10):1232-34.	37
Chapter 4	Association of the PTPN22 C1858T single nucleotide polymorphism with rheumatoid arthritis phenotypes in an inception cohort. <i>Arthritis Rheum.</i> 2005;52(9):2948-50.	43
Chapter 5	The RAGE G82S polymorphism is not associated with rheumatoid arthritis independent of HLA-DRB1*0401. <i>Rheumatology (Oxford).</i> 2006;45(4):488-90.	51
Chapter 6	Understanding the genetic contribution to rheumatoid arthritis. <i>Curr Opin Rheumatol.</i> 2005;17(3):299-304.	57
Part 2	Association between the HLA Class II alleles and autoantibodies	
Chapter 7	Refining the complex rheumatoid arthritis phenotype based on specificity of the HLA-DRB1 shared epitope for antibodies to citrullinated proteins. <i>Arthritis Rheum.</i> 2005;52(11):3433-38.	69
Chapter 8	HLA-DR3 is associated with anti-CCP antibody negative rheumatoid arthritis. <i>Arthritis Rheum.</i> 2005;52(10):3058-62.	81
Chapter 9	Smoking is a risk factor for anti-CCP antibodies only in rheumatoid arthritis patients that carry HLA-DRB1 Shared Epitope alleles. <i>Ann Rheum Dis.</i> 2006;65(3):366-71.	93
Chapter 10	The HLA-DRB1 shared epitope alleles are primarily a risk factor for anti-CCP antibodies and are not an independent risk factor to develop rheumatoid arthritis. <i>Arthritis Rheum.</i> 2006;54(4):1117-21.	105
Chapter 11	Antibodies to citrullinated proteins and differences in clinical progression of rheumatoid arthritis. <i>Arthritis Res Ther.</i> 2005;7(5):R949-58.	115

Part 3	Items of RA severity	
Chapter 12	The invasiveness of fibroblast-like synoviocytes is an individual patient characteristic associated with the rate of joint destruction in patients with rheumatoid arthritis. <i>Arthritis Rheum. 2005;52(7):1999-2002.</i>	131
Chapter 13	Variation in radiological joint destruction in rheumatoid arthritis differs between monozygotic and dizygotic twins and pairs of unrelated patients. <i>Arthritis Rheum. 2006;54(6):2028-30.</i>	139
Part 4	Prediction of the disease course in arthritis	
Chapter 14	Genetics and clinical characteristics to predict rheumatoid arthritis. Where are we now and what are the perspectives. <i>Future Rheumatology. 2006;1(1):79-89.</i>	145
Chapter 15	Arthritis of the large joints, in particular the knee, at first presentation is predictive for a high level of radiological destruction of the small joints in rheumatoid arthritis. <i>Submitted.</i>	163
Chapter 16	A rule to predict disease outcome in patients with recent-onset undifferentiated arthritis to guide individual treatment decisions. <i>Submitted.</i>	175
Chapter 17	Summary and discussion	189
Chapter 18	Nederlandse samenvatting	201
	Dankwoord	207
	Curriculum Vitae	209
	Publications	211