



Universiteit
Leiden
The Netherlands

Towards therapeutic disease control in inflammatory bowel diseases

Vos, A.C.W.

Citation

Vos, A. C. W. (2011, September 8). *Towards therapeutic disease control in inflammatory bowel diseases*. Retrieved from <https://hdl.handle.net/1887/17819>

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/1887/17819>

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

Towards therapeutic disease control in inflammatory bowel diseases

Anne Christine W. Vos

Towards therapeutic disease control in inflammatory bowel diseases

Anne Christine W. Vos

Thesis, University of Leiden

ISBN: 978-90-817740-0-0

Cover designed by Joop Bierling, Houten

Printed by Drukkerij Bariet B.V.

© 2011 A.C.W. Vos, Leiden, the Netherlands

All rights reserved. No part of this thesis may be reproduced or transmitted in any form, by any means, electronic or mechanical, without prior written permission of the author.

The printing of this thesis was financially supported by the Dutch Society of Gastroenterology (Nederlandse Vereniging van Gastroenterologie, NvGE), Section Experimental Gastroenterology (SEG) of the Dutch Society of Gastroenterology (NvGE), ABBOTT Immunology, MSD, Tramedico B.V., Ferring.

Towards therapeutic disease control in inflammatory bowel diseases

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 donderdag 8 september 2011
klokke 15.00 uur

door

Anne Christine W. Vos

geboren te Utrecht

in 1985

Promotiecommissie

Promotor:

Prof. dr. D.W. Hommes

Co-Promotores:

Dr. G.R. van den Brink

Dr. M.E. Wildenberg

Overige leden:

Prof. dr. S. Vermeire, Universitair Ziekenhuis Gasthuisberg, Leuven

Prof. dr. G. D'Haens, Academisch Medisch Centrum, Amsterdam

Prof. dr. M.P. Peppelenbosch, Erasmus MC, Rotterdam

Prof. dr. S.J. van Deventer, Leids Universitair Medisch Centrum

Prof. dr. F. Koning, Leids Universitair Medisch Centrum

List of abbreviations

3-MA	3-methyladenine
5-ASA	5-aminosalicylic acid
6-MP	6-mercaptopurine
6-TG	6-thioguanine
ADA	adalimumab
ADCC	antibody-dependent cellular toxicity
AIEC	adherent-invasive E. coli
APC	antigen presenting cell
ASCA	anti-Saccharomyces cerevisiae
ATG16L1	autophagy-related 16-like 1
AZA	azathioprine
BMDC	bone marrow derived dendritic cells
CARD15	caspase recruitment domain family, member 15
CCMO	Central Committee on Research involving Human Subject
CD	Crohn's disease
CDAI	Crohn's disease activity index
CDEIS	Crohn's disease index of severity
CEACAM6	Carcinoembryonic antigen-related cell adhesion molecule 6
CI	confidence interval
CMV	cytomegalovirus
CRP	C reactive protein
DC	dendritic cell
E. Coli	Escheria Coli
EBV	Epstein-barr virus
ESR	erythrocyte sedimentation rate
FDA	food and drug administration
FSC	forward scatter
GFP	green fluorescent protein
GvHD	Graft versus host disease
GWAS	Genome Wide Association Study
HBV	hepatitis B virus
HL	Hodgkin lymphoma
HSV	herpes simplex virus
HVI	Harvey Bradshaw Index
I2	CD associated bacterial sequence
IBDU	unspecified inflammatory bowel disease
ICAM-1	Inter-Cellular Adhesion Molecule 1
IDO	indoleamine 2,3-dioxygenase
IFN γ	interferon- γ
IFX	infliximab

Ig	immunoglobulin
IL	interleukin
INH	isonicotinylhydrazine
IRGM	immunity-related GTPase family M
IS	immunological synapse
LAMP-2	lysosomal-associated membrane protein 2
LFA-1	lymphocyte function-associated antigen 1
LPMNC	lamina propria mononuclear cell
LPS	lipopolysaccharide
LTA	lymphotoxin-alpha
MDP	muramyl dipeptide
MHC	major histocompatibility complex
MMP	matrix metalloproteinase
MSC	mesenchymal stromal cell
mTNF	membrane bound tumor necrosis factor alpha
M ϕ	macrophage
M ϕ 1	type 1 macrophage
M ϕ 2	type 2 macrophage
NHL	non-Hodgkin lymphoma
NOD	nucleotide-binding oligomerization domain
OmpC	Escheria coli outer membrane porin C
PBMC	peripheral blood mononuclear cell
PCR	polymerase chain reaction
PD-L1	programmed cell death 1 ligand 1
Pi	propidium iodide
PML	multifocal leukoencephalopathy
RA	rheumatoid arthritis
RR	relative risk
SES-CD	simple endoscopic score for Crohn's disease
SNP	single nucleotide polymorphism
SSC	side scatter
STAT3	signals transducer and activator of transcription 3
TACE	tumor necrosis factor alpha converting enzyme
TB	tuberculosis
TCR	T cell receptor
TGF β	tumor growth factor
TIMP	tissue inhibitor of metalloproteinases
TLR	toll-like receptor
TNFSF15	tumor necrosis factor superfamily 15
TNF α	tumor necrosis factor alpha
Tregs	regulatory T cells
UC	ulcerative colitis
VCAM-1	vascular cell adhesion molecule 1

Contents

Chapter 1	General Introduction	9
Chapter 2	Early intensive treatment for Crohn's disease <i>Springer IBD text book, under review</i>	33
Chapter 3	Dendritic cell autophagy attenuates adaptive immune responses by destabilization of the immunological synapse <i>Manuscript in preparation</i>	51
Chapter 4	Anti-TNF antibodies induce regulatory macrophages in an Fc region dependent manner <i>Gastroenterology. 2011;140:221-230</i>	73
Chapter 5	Regulatory macrophages induced by infliximab are involved in healing <i>in vivo</i> and <i>in vitro</i> <i>Inflammatory Bowel Diseases. Accepted for publication</i>	95
Chapter 6	Autologous bone marrow derived mesenchymal stromal cell treatment for refractory luminal Crohn's disease: results from a phase I study <i>Gut. 2010;59:1662-1669</i>	109
Chapter 7	Risk of malignant lymphoma in patients with Inflammatory bowel diseases, a Dutch nation-wide study <i>Inflammatory Bowel Diseases. 2010 Dec 22. [Epub ahead of print]</i>	129
Chapter 8	Summarizing discussion	145
Chapter 9	Appendices Nederlandse samenvatting voor niet-ingewijden List of publications Curriculum vitae Nawoord Full colour illustrations	153



The illustrations marked with this icon, can also be found in Chapter 9, 'Full colour illustrations'.

