

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/28731> holds various files of this Leiden University dissertation

**Author:** Majowicz, Anna

**Title:** Addressing immune tolerance issues in inflammatory bowel disease and adeno-associated virus based gene transfer

**Issue Date:** 2014-09-17

**Addressing immune tolerance issues  
in inflammatory bowel disease and  
adeno-associated virus based gene transfer**

**Anna Majowicz**

---

PhD Thesis, Leiden University, September 2014

Addressing immune tolerance issues in inflammatory bowel disease and adeno-associated virus based gene transfer

ISBN: 978-90-9028477-4

Layout: Anna Majowicz

Cover:: Anna Majowicz

Printed by TPM, Rzeszów

Copyright © 2014, Anna Majowicz. All rights reserved. No part of this thesis may be reproduced or transmitted in any form, by any means, without prior written permission of the author.

The printing of this thesis was financially supported by:

uniQure

Leiden University Medical Center

BD Biosciences

---

**Addressing immune tolerance issues  
in inflammatory bowel disease and  
adeno-associated virus based gene transfer**

Proefschrift

ter verkrijging van  
de grad van Doctor aan de Universiteit Leiden,  
op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker  
volgens besluit van het College voor Promoties  
te verdedigen op woensdag 17 september 2014

klokke 10:00 uur

door

**Anna Majowicz**

geboren te Krosno (Polen)

in 1983

**PROMOTIECOMMISSIE:**

Promotor: Prof. Dr. Sander J. H. van Deventer

Co-promotores: Dr. Valerie Ferreira (uniQure, Amsterdam)  
Dr. Harald Petry (uniQure, Amsterdam)

Overige leden: Prof. Dr. Pieter H. Reitsma  
Prof. Dr. Bart van Hoek  
Dr. Ir. Hein W. Verspaget  
Prof. Dr. Gijs R. van den Brink (Academic Medical Center,  
Amsterdam)  
Associate Prof. Dr. Federico Mingozi (University Pierre and  
Marie Curie, Paris)

Faculteit der Geneeskunde

# **Contents**

### Part I

<b>Chapter 1</b>	<b>Introduction Part I</b>	15
	Gene and cell therapy based treatment strategies for inflammatory bowel diseases (van der Marel, S., Majowicz, A., van Deventer, S. J. H., Petry, H., Hommes, D. W., and Ferreira, V., 2011, <i>World J. Gastrointest. Pathophysiol.</i> ; 2: 114-122).	
<b>Chapter 2</b>	Generation of stable, functional regulatory T lymphocytes <i>in vitro</i> within 4 days by a two step activation protocol (van der Marel, S., Majowicz, A., Ferreira, V.)	39
<b>Chapter 3</b>	Murine CD4(+)CD25(-) cells activated <i>in vitro</i> with PMA/ionomycin and anti-CD3 acquire regulatory function and ameliorate experimental colitis <i>in vivo</i> (Majowicz, A., van der Marel, S., te Velde, A. A., Meijer, S. L., Petry, H., van Deventer, S. J. H., and Ferreira, V., 2012, <i>BMC Gastroenterol.</i> ; 12: 172).	61
<b>Chapter 4</b>	Adeno-associated virus mediated delivery of Tregitope 167 ameliorates experimental colitis (van der Marel, S., Majowicz, A., Kwikkers, K. L., van Logtenstein, R., te Velde, A. A., De Groot, A. S., Meijer, S. L., van Deventer, S. J. H., Petry, H., Hommes, D. W., and Ferreira, V., 2012, <i>World J. Gastroenterol.</i> ; 18: 4288-4299).	81

## **Part II**

<b>Chapter 5</b>	<b>Introduction Part II</b>	107
	Overcoming AAV immunogenicity (Majowicz, A., Ferreira, V.)	
<b>Chapter 6</b>	Successful re-administration of adeno-associated virus (AAV) vectors: cross administration of AAV serotypes 5 and 1 (Majowicz, A., Ferreira, V.)	129
<b>Chapter 7</b>	Use of immunosuppressive regimens to reduce humoral immunogenicity generated by primary AAV vector delivery (Majowicz, A., van der Marel, S., Ferreira, V.)	143
<b>Chapter 8</b>	Mir-142-3p target sequences reduce transgene directed immunogenicity following intramuscular AAV vector-mediated gene delivery (Majowicz, A., Maczuga, P., Kwikkers, K. L., van der Marel, S., van Logtenstein, R., Petry, H., van Deventer, S. J. H., Konstantinova, P., and Ferreira, V., 2013, <i>J. Gene Med.</i> ; 15: 219-232).	159
<b>Chapter 9</b>	General discussion	187
<b>Addendum</b>	Nederlandse samenvatting Streszczenie Curriculum Vitae Publications Acknowledgements List of abbreviations	199

