



**Universiteit  
Leiden**  
The Netherlands

## **From immune suppression to immune modulation in type 1 diabetes patients**

Megen, K.M. van

### **Citation**

Megen, K. M. van. (2021, October 5). *From immune suppression to immune modulation in type 1 diabetes patients*. Retrieved from <https://hdl.handle.net/1887/3214562>

Version: 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/1887/3214562>

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

From Immune Suppression  
to Immune Modulation  
in Type 1 Diabetes Patients

Kayleigh Montana van Megen

# From Immune Suppression To Immune Modulation in Type 1 Diabetes Patients

Proefschrift

© 2021 K.M. van Megen, Leiden, the Netherlands

From immune suppression to immune modulation in type 1 diabetes patients

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

The research presented in this thesis was performed at the City of Hope Beckman Research Institute in Duarte, California, in conjunction with the University of Leiden.

Financial support for the publication of this thesis was kindly provided by Chipsoft and Stichting Diabetes Onderzoek Nederland (DON).

Cover and Illustrations: K.M. van Megen

Printed by: Drukkerij Ruparo, Amsterdam

ISBN: 9789090351438

ter verkrijging van  
de graad van doctor aan de Universiteit Leiden,  
op gezag van rector magnificus prof. dr. ir. H. Bijl,  
volgens besluit van het college voor promoties  
te verdedigen op dinsdag 5 oktober 2021,  
klokke 11:15 uur

door

**Kayleigh Montana van Megen**

Geboren te Amsterdam, Nederland

in 1991

voor

Vincent, Hans-Peter, en Dante

Promotores: Prof. Dr. B.O. Roep

Prof. Dr. J.J. Zwaginga

Co-promotor: Dr. T. Nikolic

Leden promotiecommissie: Prof. Dr. E.J.P. de Koning

Prof. Dr. C. Mathieu (Klinische en Experimentele  
Endocrinologie, KU Leuven, België)

Dr. H.J. Aanstoot (Senior Medical Director en kinderarts  
bij Diabeter Rotterdam, Nederland)

Prof. Dr. J. de Vries (Translatieele Tumurimmunologie,  
Radboud Universiteit)

*To develop a complete mind:*

*Study the science of art;*

*Study the art of science.*

*Learn how to see.*

*Realize that everything connects to everything else.*

---

– Leonardo da Vinci (1452-1519)

## Contents

Chapter 1: Introduction	2
-------------------------	---

---

### ***PART I: TYPE 1 DIABETES CAN BE REVERSED BY IMMUNOTHERAPY***

---

Chapter 2: A future for autologous hematopoietic stem cell transplantation in type 1 diabetes	26
Chapter 3: Relapsing/remitting type 1 diabetes	38

---

### ***PART II: USING ANTIGEN-PRESENTING CELLS TO REINSTATE IMMUNE BALANCE IN T1D***

---

Chapter 4: 1,25(OH) <sub>2</sub> Vitamin D3 induces stable and reproducible therapeutic tolerogenic dendritic cells with specific epigenetic modifications	50
Chapter 5: Activated MSCs process and present antigens regulating adaptive immunity	98

---

### ***PART III: RECOVERING THE IMMUNE BALANCE IN ISLETS OF LANGERHANS***

---

Chapter 6: Intra-pancreatic tissue-derived mesenchymal stromal cells: a promising therapeutic potential with anti-inflammatory and pro-angiogenic profiles	122
--	-----

---

### ***PART IV: DISCUSSION & SUMMARIES***

---

Chapter 7: General Discussion	148
Chapter 8: Summaries (English & Dutch)	170
List of publications	181
Acknowledgments	182
Curriculum Vitae	185