



Universiteit  
Leiden  
The Netherlands

## Mass spectrometry-based degradomics analysis of toxoid vaccines

Michiels, T.J.M.

### Citation

Michiels, T. J. M. (2021, September 9). *Mass spectrometry-based degradomics analysis of toxoid vaccines*. Retrieved from <https://hdl.handle.net/1887/3209234>

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/1887/3209234>

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

Cover Page



Universiteit Leiden



The handle <https://hdl.handle.net/1887/3209234> holds various files of this Leiden University dissertation.

**Author:** Michiels, T.J.M.

**Title:** Mass spectrometry-based degradomics analysis of toxoid vaccines

**Issue Date:** 2021-09-09

# **MASS SPECTROMETRY-BASED DEGRADOMICS ANALYSIS OF TOXOID VACCINES**

**Thomas Michiels**

*Cover design:* Thomas Michiels & Gildeprint

*Cover photos:* Wil Michiels & Lidy van Staalduin

*Thesis lay-out:* Wendy Bour-van Telgen

*Printing:* Gildeprint

© Copyright, Thomas Michiels, 2021

ISBN: 978-94-6419-267-4

All rights reserved. No part of this book may be reproduced in any form or by any means without permission of the author.

# **MASS SPECTROMETRY-BASED DEGRADOMICS ANALYSIS OF TOXOID VACCINES**

**Proefschrift**

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 donderdag 9 september 2021

klokke 13.45 uur

Door

Thomas Joost Martti Michiels

geboren te Roosendaal en Nispen

In 1991

**Promotores:** Prof. Dr. G.F.A. Kersten

Prof. Dr. W. Jiskoot

**Co-promotor:** Dr. B. Metz

**Promotiecommissie:** Prof. Dr. H. Irth, Universiteit Leiden (voorzitter)

Prof. Dr. J.A. Bouwstra, Universiteit Leiden (secretaris)

Prof. Dr. E.M. Topp, Purdue University

Prof. Dr. C.A.C.M. van Els, Universiteit Utrecht

Prof. Dr. C.F.M. Hendriksen, Universiteit Utrecht

The research described in this thesis was performed at the Institute for Translational Vaccinology, Intravacc (Bilthoven, the Netherlands) and the division BioTherapeutics of the Leiden Academic Centre for Drug Research (LACDR), Leiden University (Leiden, The Netherlands). The research was financially supported in part by the Vac2Vac project supported by the Innovative Medicines Initiative2 Joint Undertaking under grant agreement N-115924 and by the Ministry of Agriculture, Nature, and Food Quality, the Netherlands.

## Table of contents

<b>Chapter 1</b>	General introduction and thesis outline	7
<b>Chapter 2</b>	Identification of formaldehyde-induced modifications in diphtheria toxin	21
<b>Chapter 3</b>	Formaldehyde treatment of proteins enhances proteolytic degradation by the endo-lysosomal protease cathepsin S	61
<b>Chapter 4</b>	Novel formaldehyde-induced modifications of lysine residue pairs in peptides and protein: identification and relevance to vaccine development	85
<b>Chapter 5</b>	Degradomics-based analysis of tetanus toxoids as a quality control assay	113
<b>Chapter 6</b>	Common reference-based tandem mass tag multiplexing for the relative quantification of peptides: design and application to degradome analysis of diphtheria toxoid	135
<b>Chapter 7</b>	Summary, general discussion and prospects	153
<b>Appendix</b>	Nederlandstalige samenvatting	166
	List of publications	168
	Curriculum vitae	170

