



Universiteit
Leiden
The Netherlands

Development of hyaluronan-based dissolving microneedle arrays for dermal vaccination

Leone, M.

Citation

Leone, M. (2020, December 10). *Development of hyaluronan-based dissolving microneedle arrays for dermal vaccination*. Retrieved from <https://hdl.handle.net/1887/138252>

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/1887/138252>

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

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/138252> holds various files of this Leiden University dissertation.

Author: Leone, M.

Title: Development of hyaluronan-based dissolving microneedle arrays for dermal vaccination

Issue date: 2020-12-10

Development of hyaluronan-based dissolving microneedle arrays for dermal vaccination

Mara Leone

Development of hyaluronan-based dissolving microneedle arrays for dermal vaccination

PhD thesis with summary in Dutch

©2020 Mara Leone. All rights reserved. No part of this thesis may be reproduced or transmitted in any form or by any means without written permission of the author.

Cover : the fluorescence microscopy images provide a view parallel to the skin surface and depict fluorescein amine-labeled hyaluronan (green), rhodamine B-labeled trimethyl chitosan (white) and lumogallion-labeled diphtheria toxoid (red) released in *ex vivo* human skin.

Cover design: Mara Leone

Printing: Off Page, Amsterdam

ISBN: 978-94-93197-35-0

Development of hyaluronan-based dissolving microneedle arrays for dermal vaccination

PROEFSCHRIFT

ter verkrijging van

de graad van Doctor aan de Universiteit Leiden,

op gezag van de Rector Magnificus prof.mr. C.J.J.M. Stolker,

volgens besluit van het College voor Promoties

te verdedigen op donderdag 10 december 2020

klokke 10:00 uur

door

Mara Leone

Geboren te Avellino, Italy

in 1987

Promotoren Prof. Dr. G.F.A. Kersten
Prof. Dr. J.A. Bouwstra

Promotiecommissie Prof. Dr. H. Irth, Universiteit Leiden (voorzitter)
Prof. Dr. A. P. IJzerman, Universiteit Leiden (secretaris)
Prof. Dr. C. W. J. Oomens, Universiteit Eindhoven
Prof. Dr. Ir. W. E. Hennink, Universiteit Utrecht
Prof. Dr. A.L.W. Huckriede, Rijksuniversiteit Groningen
Dr. A. Moore, University College Cork, Ireland

The research described in this thesis was performed at the division BioTherapeutics of the Leiden Academic Centre for Drug Research (LACDR), Leiden University (Leiden, The Netherlands). The research was financially supported by Intravacc (Bilthoven, The Netherlands).

To my family,
to Paolo,
for being always by my side
giving me strength, support and endless love

TABLE OF CONTENTS

Chapter 1

General introduction, aim and outline of this thesis 1

Chapter 2

Dissolving Microneedle Patches for Dermal Vaccination 9

Chapter 3

Universal Applicator for Digitally-Controlled Pressing Force and Impact Velocity Insertion of Microneedles into Skin..... 41

Chapter 4

Hyaluronan-based dissolving microneedles with high antigen content for intradermal vaccination: Formulation, physicochemical characterization and immunogenicity assessment 67

Chapter 5

Hyaluronan molecular weight: Effects on dissolution time of dissolving microneedles in the skin and on immunogenicity of antigen..... 99

Chapter 6

Diphtheria toxoid dissolving microneedle vaccination: adjuvant screening and effect of repeated-fractional dose administration 119

Chapter 7

Summarizing discussion and prospects..... 147

Appendices

Nederlandse samenvatting 157

Curriculum Vitae..... 165

List of publications 167

