

University of Groningen

Pemphigus pathogenesis

Sokol, Ena

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2016

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Sokol, E. (2016). *Pemphigus pathogenesis: Insights from light and electron microscopy studies*. University of Groningen.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Pemphigus pathogenesis

Insights from light and electron microscopy studies

Ena Sokol

2016



The research presented in this thesis was performed at the Department of Cell Biology and Department of Dermatology, University Medical Center Groningen, University of Groningen, The Netherlands. The work was financially supported by Erasmus Mundus Action 2 programme (JoinEU-SEE) and University of Groningen. Advanced Imaging was sponsored by ZonMW 91111.006; NWO 175-010-2009-023 and STW "Microscopy Valley" 12718.

Financial support for the publication of this thesis was provided by: Graduate School of Medical Sciences, University of Groningen; Stichting Studiefonds Dermatologie, University Medical Center Groningen; Fagron B.V.

Cover design, chapter pages and bookmark: Bianca Pijl, www.pijlldesign.nl
Printed by: Ipskamp Drukkers, Enschede, The Netherlands

ISBN: 978-94-6259-982-6

Copyright©2016 by Ena Sokol. All rights reserved. No part of this book may be reproduced in any form without permission from the author.



**rijksuniversiteit
 groningen**

Pemphigus pathogenesis

Insights from light and electron microscopy studies

Proefschrift

ter verkrijging van de graad van doctor aan de
Rijksuniversiteit Groningen
op gezag van de
rector magnificus prof. dr. E. Sterken
en volgens besluit van het College voor Promoties

De openbare verdediging zal plaatsvinden op

woensdag 6 januari 2016 om 14.30 uur

door

Ena Sokol

geboren op 19 januari 1986
te Banja Luka, Bosnië en Herzegovina

Promotor

Prof. dr. M.F. Jonkman

Copromotores

dr. H.H. Pas

dr. B.N.G. Giepmans

Beoordelingscommissie

Prof. dr. P.J. Peters

Prof. dr. R. Ludwig

Prof. dr. P. Heeringa

Contents

	List of abbreviations	7
Chapter 1	Introduction	9
Chapter 2	Large-scale electron microscopy maps of patient skin and mucosa provide insight into pathogenesis of blistering diseases	59
Chapter 3	Desmoglein 1 in pemphigus foliaceus patient skin is depleted from desmosomes, clustered in interdigitating double membrane structures and sequestered in large cytoplasmic vesicles	77
Chapter 4	Pemphigus vulgaris autoantibodies cause invaginations of one cell into another	93
Chapter 5	Discussion and future perspectives	111
Chapter 6	Summary/Samenvatting/Sažetak	119
References		129
Acknowledgments		143
About the author		148

List of abbreviations

PV	pemphigus vulgaris
mdPV	mucosal dominant pemphigus vulgaris
mcPV	mucocutaneous pemphigus vulgaris
PF	pemphigus foliaceus
SSSS	staphylococcal scalded skin syndrome
Dsg	desmoglein
Dsc	desmocollin
Pg	plakoglobin
Plk	plakophilin
Dp	desmoplakin
ECD	extracellular core domain
IDP	inner dense plaque
ODP	outer dense plaque
EM	electron microscopy
CLEM	correlative light and electron microscopy
PK	primary keratinocytes
N+	Nikolsky positive
IgG	immunoglobulin G



Chapter 1

Introduction

Contents

Chapter 1A	Structure of desmosomes	11
Chapter 1B	Desmosomal diseases and non-adhesive roles of desmosomal proteins	17
Chapter 1C	Pemphigus: disease and pathogenesis	39
Thesis aim		57