

University of Groningen

Revertant cell therapy for epidermolysis bullosa

Gostynski, Antoni

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:
2014

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

Citation for published version (APA):

Gostynski, A. (2014). *Revertant cell therapy for epidermolysis bullosa*. [Thesis fully internal (DIV), University of Groningen]. [S.n.].

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).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

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.

Revertant cell therapy for epidermolysis bullosa

A.H. Gostyrński

2014

ISBN: 978-90-367-7442-0

ISBN: 978-90-367-7441-3 (e-book)

© Copyright 2014 A.H. Gostynski, The Netherlands

All rights reserved. No part of this thesis may be reproduced, stored in a retrieval system or transmitted in any form or by any means, without prior permission of the author.

Financial support for the publication of this thesis was provided by:

AbbVie BV, AllWeCare medical BV, Almirall BV, Department of Dermatology and Schiting Stiefonds Dermatologie, UMCG, Fagron BV, Galderma, Graduate School of Medicine Groningen (GUIDE), LEO Pharma BV, Medizorg BV, University of Groningen, Urgo medical, Will-Pharma BV

Financial support by Vlinderkind and J.P. Nater Foundation for the research described in this thesis is gratefully acknowledged.

Design & Layout: M.O. Wolf, MOTTOW (mottow.nl), Groningen, The Netherlands



university of
 groningen

REVERTANT CELL THERAPY FOR EPIDERMOLYSIS BULLOSA

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 17 december 2014 om 9:00 uur

door

Antoni Henryk Gostyrński

geboren op 5 juni 1984
te Lublin, Polen

Promotor: Prof. dr. M.F. Jonkman

Copromotor: Dr. ir. A.M.G. Pasmooij

Beoordelingscommissie: Prof. dr. D.R. Roop
Prof. dr. J. Schalkwijk
Prof. dr. P.M.N. Werker

For
my Mom, for teaching me to always ask *why*,
my Wife, for tolerating, supporting and stimulating all my *whys*,
and my Daughter, for becoming my *why*.

LIST OF ABBREVIATIONS

AF	anchoring fibrils
BMZ	basement membrane zone
Col17	type XVII collagen
Col7	type VII collagen
DEB	dystrophic epidermolysis bullosa
DMEM	Dulbecco's modified Eagle's medium
EB	epidermolysis bullosa
EDTA	ethylenediaminetetraacetic acid
GMP	good manufacturing practice
HBEGF	heparin-binding epidermal growth factor
HFSC	hair follicle stem cells
HMGB1	high mobility group box 1 protein
IF	immunofluorescence
6 iPSC	induced pluripotent stem cell
JEB	junctional epidermolysis bullosa
JEB-gen-intermed	JEB, generalized intermediate (earlier JEB-non Herlitz) type
JEB-gen-sev	JEB generalized severe (earlier JEB-Herlitz) type
JEB-loc	JEB, localized type
lam-332	laminin-332
mAb	monoclonal antibody
MelSC	melanocyte stem cells
PBS	phosphate buffered saline
PCR	polymerase chain reaction
RDEB	recessive dystrophic epidermolysis bullosa
RDEB-gen-sev	RDEB, generalized severe type
RM	revertant mosaicism
SCC	squamous cell carcinoma
TA	transient amplifying
TALEN	transcription activator like effector nucleases
WAS	Wiskott-Aldrich Syndrom
ZFN	zinc-finger nucleases

TABLE OF CONTENTS

Chapter 1	Introduction	9	
Chapter 2	Adhesive stripping to remove epidermis in junctional epidermolysis bullosa for revertant cell therapy	47	
Chapter 3	Long-term survival of type XVII collagen revertant cells in an animal model of revertant cell therapy	55	
Chapter 4	Successful therapeutic transplantation of revertant skin in epidermolysis bullosa	65	
Chapter 5	Pigmentation and melanocyte supply to the epidermis depend on type XVII collagen	73	7
Chapter 6	Not all roads lead to successful revertant cell therapy	87	
Chapter 7	General discussion and future perspectives	99	
Chapter 8	Summary	115	
Chapter 9	Samenvatting	123	
Appendices	Acknowledgements	132	
	List of publications	136	
	Curriculum Vitae	137	

