

University of Groningen

Substantiating atypical phenotypes of epidermolysis bullosa

Gostynska, Katarzyna Barbara

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):

Gostynska, K. B. (2016). *Substantiating atypical phenotypes of epidermolysis bullosa*. [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit 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).

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.

Appendices

Acknowledgements
List of publications
Curriculum Vitae

ACKNOWLEDGEMENTS

Completing this thesis has been an incredible, challenging, and ultimately very rewarding milestone in my career. The entire process from start to finish could not have been realized without the involvement of many wonderful people. As such, I would like to take the opportunity to thank them here.

To begin with, my promotor, Prof. dr. M.F. Jonkman. Dear Marcel, thank-you for giving me the chance to realize my dream to become a dermatologist. Not only did you accept me enter the Groningen residency program, but along the way gave me the chance to undertake EB research on a World class level. To be the best, one must learn from the best. Thank-you for your continual support, motivation and for making these projects a priority when they needed to be. I am very proud of all that we have achieved!

My second promotor, Prof. dr. Richard Sinke. Dear Richard, you introduced me to the world of DNA diagnostics and taught me the in's and out's of the human genome. I very much enjoyed all of our Friday meetings discussing the cold cases and learning about genome diagnostics. Thank-you for your mentorship and always positive humour.

My co-promotor, Dr. A.M.G. Pasmooij, Dear Marjon! When you do something, you do it 200% full on. I cannot count all of the times when you managed to review my articles or results of experiments from the spot from which you were currently vacationing. Thank-you for being my mentor in all aspects of RNA experiments, writing scientific articles and brainstorming. I very much enjoyed all of the conferences in Venice, Marbella, and Scotland. You have become a dear friend, thank-you for everything!

I would like to thank all the members of the reading committee. Prof. dr. Cristina Has, Prof. dr. Rolf H. Sijmons, and Prof. dr. Pieter Steijlen, thank-you for reading and judging my thesis.

This thesis was done in collaboration with the Department of Genetics of the UMCG. I am indebted to the staff for their help and input in my research. Firstly, to Dr.H. Lemmink, Dear Henny, thank-you for teaching me everything about DNA sequencing and brainstorming over the cold cases. Without you, Chapter 3 would not have turned out the way it did! 'Our' clinical geneticist Dr. van den Akker. Dear Peter, I am grateful for your continual interest in my projects and for always offering your advice and critical check on the manuscripts. It is truly a great pleasure to work together with you! Thank-you for making it back to Groningen for June 6th!

Krista van Dijk Bos, Birgit Sikkema-Raddatz and Lennart Johansson thank-you for always making me feel welcome in the department of Genetics and for teaching me everything I know about NGS technology.

This PhD could not have been possible without a truly solid Immunodermatology lab. First of all, our boss, Dr. H. H. Pas. Dear Hendri, from the very beginning, your guidance surrounding lab work, immunoblot and ELISAs defined the functional studies. Thank-you!

Jeroen Bremer, thank-you for your input in my projects, all of the PCR's and sequencing studies without which we could have literally not substantiated any of the atypical phenotypes.

Miranda Nijenhuis, you guided me through my first ever PCR with much patience and were always enthusiastic about my work. Without you, Chapter 2 would not have been possible, thank-you!

Dr. Gilles Diercks, our dermatopathologist. I appreciate all of your advice on electron microscopy, immunofluorescence antigen mapping and histopathology of EB!

Janny Zuiderveen, Gonnie Meijer, Laura Vos and Duco Kramer, countless immunofluorescence coupes, TEM slides, ELISAs, immunoblots would not have been possible without all of you. Thank-you for contributing to my projects.

Thank-you to our international collaborators in Vienna, Prof. Gerhard Wiche and Dr. Maria Castañón whose hard work resulted in the excellent Plectin 1a manuscript presented in Chapter 2. Additionally, thank-you to Dr. Kernland Lang from Bern, who also collaborated on this project.

José Duipmans, our EB Nurse Practitioner. Over the past couple of years I have learned so much from you about the everyday care of patients affected with EB. It is truly inspiring to work with someone who puts their heart into everything they do. Thank-you for everything!

Many thanks to the Groningen multidisciplinary EB team, in particular our maxillofacial surgeon, Dr. Kees Stellingsma. Dear Kees, I appreciate all of your dental expertise which completed Chapter 5!

Dr. Marieke Bolling and Dr. Wing Yan Yuen, it was a great honor to follow in both of your footsteps in genetics research of EB. Additionally, I would like to thank all of the PhD fellows at the department of dermatology who work in EB, autoimmune blistering diseases, eczema and hidradenitis suppurativa is truly exemplary!

During my research I had the opportunity to meet and treat many EB patients, whose positive attitude and outlook on life were unlike anything I have ever encountered. To everyone affected with EB, thank-you for participating in the studies, offering your help and for being there for us!

An enormous thank-you goes out to the EB patient organizations, both national and international, Debra Nederland, Debra International and Vlinderkind for always supporting our work.

My two lovely paranymfs, Dr. J.L. Dickinson-Blok and Dr. I.C. Janse! Both of you were with me, day in and day out in different moments of this research, while at the same time finishing both of your own manuscripts. Thank-you for all of the moments together, for advice, and for understanding what it all truly is all about. Dear Janine, your friendship has been the best side effect of this PhD and I am truly fortunate to have you as a dear friend. Dear Ineke, we began residency together in 2011, and now complete this milestone 1 week apart. You both set the example of how it should be done and helped me in so many ways at the end. Thank-you for being with me on June 6th!

Although not mentioned in this book, the majority of my PhD time was spent on setting up a novel therapy for severe forms of epidermolysis bullosa. I would like to express my gratitude for the collaboration with stem cell transplantation experts Dr. Jaap Jan Boelens and Dr. Caroline Lindemans in the Wilhelmina Childrens Hospital in Utrecht. Thank-you for opening up allogeneic stem cell transplantation to inherited skin disease in Europe. We have worked very,very hard over the past couple of years, and I feel that the best is yet to come.

Tying into this, I am grateful for our outstanding international collaboration with Prof. Dr. John McGrath, Dr. Jakub Tolar, Dr. Anna Martinez, Dr. Jemma Mellerio and Prof. Christine Bodemer on research of EB.

Prof. Marek Haftek in Lyon. My first ever performed immunofluorescence antigen mapping was in beautiful Lyon where I came to learn about skin research as a medical student. Who knew that it would become such an important aspect of my career. Thank-you for introducing me to skin research at INSERM and together with your family for showing me the beauty of Plateau. I cannot wait to come back. Merci merci merci!

My residency director, Dr. Barbara Horváth. Polak, Węgier, dwa bratanki, i do szabli, i do szklanki (Lengyel, Magyar – két jó barát, együtt harcol, s issza borát) Dear Barbara, thank-you for your encouragement, support and for teaching me how to treat skin disease.

Dr. Marie-Louise Schuttelaar, our Chef de Clinique. Thank-you for giving me room in the clinic to finish this thesis.

All of the staff dermatologists in UMCG, past and present. Thank-you for contributing to my residency and for understanding when my mind was not always focussed on the clinic while writing these chapters.

All of the Groningen Dermatology residents. Merci! I am very proud to be a part of our intelligent and dynamic group!

Many thanks to all of the administrative staff, doctor's assistants, and nurses from the Department of Dermatology. Thank-you for all of your practical help in supporting my research and a special thank-you to Anneke Wiegman for adjusting my polyclinic schedule that I had time to finish this thesis.

I am indebted to Anneke Hoekstra, Katarina Ondrekova and Alberta Oolders for arranging years of research meetings and for all of your help with the preparations surrounding the mini symposium. Thank-you Piet Toonder for your always positive attitude and help with medical photography!

Martijn Wolf, thank-you for the beautiful butterflies gracing the cover of this book and for all of your hard work putting the chapters together!

My lovely Dr. van Oosten! Dear Noor, from opleiding to babies, I am so happy we are still close! Thank-you for your friendship.

Przyjaciele w Polsce i w Holandii, dziękuję Wam za wspólne wyjazdy, weekendy i spotkania!

Moja Rodzino!

Wojtku i Michale, dziękuję Wam oraz Asi i Gosi za zainteresowanie moją pracą i ciepłe serce.

Babci Lusi i Babci Irce za wsparcie, troskę i ogromne serce dla rodziny.

Mamo Doroto, dziękuję za dodawanie ducha przez cały okres doktoratu, za ogromne serce i opiekę nad malutką, kiedy kończyłam książkę!

Mamo, Tato. Kolejny krok do przodu. Dziękuję Wam za nieustanne wsparcie, zainteresowanie i ciepłe serce. Bez Was nie osiągnęłabym tyle. Tato, jesteś dla mnie zawsze wzorem lekarza. Mamo, żebym mogła być taką inteligentną, dzielną i kochaną mamą i kobietą tak jak Ty!

Moja Wiktorio. Córeczko, jak pięknie być Twoją Mamą. Ukończenie tego doktoratu nie odbyło się bez twoich pierwszych kroczków, słów, i wielu innych cudownych wspomnień. Jesteś Naszą największą dumą i szczęściem. Idź zawsze za swoimi marzeniami. Kocham Cię!

Mój mężu, Antosiu, jesteś jedyną osobą bez której nie udałoby mi się skończyć tego doktoratu. To wyjątkowe, że możemy dzielić naszą pasję na co dzień. Dziękuję za wspólne życie, dom i miłość. Jesteś dla mnie wszystkim, skarbie!

Kasia, Groningen 2016

LIST OF PUBLICATIONS

A novel *PLEC* isoform rescues the phenotype in epidermolysis bullosa simplex

KB Gostyńska, H Lemmink, J Bremer, HH Pas, M Nijenhuis, PC van den Akker, RJ Sinke, MF Jonkman, AM Pasmooij

Excerpts resubmitted to the Journal of Investigative Dermatology

Carriers with functional null mutations in *LAMA3* have localized enamel abnormalities due to haploinsufficiency

KB Gostyńska, WY Yuen, AM Pasmooij, C Stellingsma, HH Pas, H Lemmink, MF Jonkman

Accepted for publication in the European Journal of Human Genetics.

In-frame exon skipping in *KRT5* due to novel intronic deletion causes epidermolysis bullosa simplex, generalized severe

KB Gostyńska, J Bremer, KK van Dijk-Bos, RJ Sinke, AM Pasmooij, MF Jonkman

Accepted for publication in Acta Dermato-Venereologica

Epidermolysis Bullosa Pruriginosa Excoriée: A Deceptive Pruritic Variant in Two Female Patients.

KB Gostyńska, MF Jonkman

Acta Derm Venereol. 2016 Jan 20;96(1):140-141

Mutation in exon 1a of *PLEC*, leading to disruption of plectin isoform 1a, causes autosomal-recessive skin-only epidermolysis bullosa simplex

KB Gostyńska, M Nijenhuis, H Lemmink, HH Pas, AM Pasmooij, K Kernland Lang, MJ Castañón, G Wiche, MF Jonkman

Hum. Mol. Genet., 2015 24 (11): 3155-3162

Epidermolysis bullosa pruriginosa excoriée

KB Gostyńska, MF Jonkman

Nederlands Tijdschrift voor Dermatologie en Venereologie, Volume 23, September 2013

Residents' corner July 2012. sQUIZ your knowledge! Diagnosis: Laptop induced erythema ab igne.

K Karolak, MF Jonkman

European Journal of Dermatology, 2012 Jul-Aug (4): 585-6

Coexistence of Klippel-Trenaunay-Weber syndrome with Sturge-Weber syndrome

A Terlikowska-Brzósko, **K Karolak**, M Sińczak, B Kwiek

Postępy Dermatologii i Alergologii, XXV, 2008

CURRICULUM VITAE



Katarzyna (Kasia) Gostyńska (née Karolak) was born on December 2nd 1985 in Warsaw, Poland. In her youth, she emigrated with her parents and two older brothers to Canada where she lived until completing high school at Handsworth Secondary School in North Vancouver, B.C.

At 17, she returned to her native Poland to study medicine at the II Medical Faculty of the Medical University of Warsaw. She obtained her MD title in 2009 and worked as a medical intern in Międzyzyleski Szpital Specjalistyczny in Warsaw, Poland until 2010. She moved to Groningen, the Netherlands in 2011 and began her residency in Dermatology and Venereology in July, 2011. In July 2012 she briefly stepped out of clinical work to pursue research on the works presented in this thesis under the supervision of Prof. dr. Marcel Jonkman, Prof. dr. Richard Sinke, Dr. Marjon Pasmooij. Concurrently she was and continues to be the coordinating investigator of a clinical trial on hematopoietic stem cell therapy for children affected with severe epidermolysis bullosa in collaboration with the Wilhelmina Children's Hospital of the University of Utrecht, Utrecht the Netherlands. In July 2014, she resumed her clinical residency. Her interests in dermatology include pediatric dermatology and genodermatoses. Kasia currently lives in Groningen with her husband Antoni and their daughter Wiktoria.

