Predicting the response of keratinocytes to damage of the epidermal barrier in atopic dermatitis

Published: 28/02/2016

Document Version
Accepted manuscript including changes made at the peer-review stage

Please check the document version of this publication:
• A submitted manuscript is the author's version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

Citation for published version (APA):

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal

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.
Predicting the Response of Keratinocytes to Damage of the Epidermal Barrier in Atopic Dermatitis

Z.C. Félix Garza¹, E.P.F. van den Biggelaar¹, J. Liebmann², M. Born², P.A.J. Hilbers¹, N.A.W. van Riel¹
¹Department of Biomedical Engineering, Eindhoven University of Technology, The Netherlands. ²Philips GmbH, Innovative Technologies, Aachen, Germany.

Atopic dermatitis (AD) is a chronic, multifactorial, inflammatory skin disease characterized by dry, itchy areas of thick epidermis known as flares. It is the result of interactions between environmental and genetic factors that cause the breakdown of the epidermal barrier and induce an inflammatory response. Consequently, keratinocytes increase their proliferation rates and differentiate atypically. Several studies suggest that changes in the barrier function may drive the activity of AD, thus leading to inflammation and the development of flares. It is hypothesized that severe insults to the epidermal barrier alone yield the generation of lesional epidermis with an increased cell density, an enlarged proliferative compartment and a decreased barrier function. In this work, we test this hypothesis using computational modeling to study the kinetics of keratinocytes and the impact of the epidermal barrier strength on these cells. The model accounts for the cellular processes of proliferation, differentiation, apoptosis and desquamation. The response of keratinocytes to barrier impairment indicates that the epidermal phenotype changes when the damage applied to the outermost layer of the epidermis surpasses a threshold. Thus lowering the barrier function, increasing the cell density, and inducing a flare of AD. Additional data is required for validation of the model predictions. The proposed computational approach is a flexible novel tool that can be used for testing the effect of different factors and treatments on the activity of AD.

Acknowledgements. This study was supported by Philips Research, Eindhoven, The Netherlands