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

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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.

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