ABSTRACT

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Podium Title: *A new 3D microbiotic skin model to reproduce the whole pathophysiological Atopic Dermatitis features*

Background information (Short introduction)

Atopic dermatitis (AD) is a multifactorial disease associated with epidermal barrier disruption, microbial imbalance with a dominance of Staphylococcus aureus and inflammatory type 2 (Th2) immune reaction. In vitro models reproducing some features of AD have previously been developed by challenging epidermis with interleukin cocktails or S. aureus extracts, or by silencing the expression of pivotal epidermal barrier proteins. But none of them reproduced the whole pathophysiological AD features.

Objective

In order to better mimic AD, we aim to develop a reconstructed human epidermis (RHE) model exposed to both a cocktail of cytokines and S. aureus.

Methodology

RHEs produced from normal human keratinocytes were treated from day 5 to 11 with a cocktail of IL-4, IL-13, IL-31 and TNF-alpha. IL-4 and IL-13 were used as major cytokines driving inflammation in AD. We also added IL-31, a potent pruritogenic cytokine primarily produced by Th2 cells, because its serum levels correlate with both the SCORAD severity score and the expression of IL-4 and IL-13. The cocktail was further supplemented with TNF-alpha, a pro-inflammatory cytokine whose production may be stimulated by IL-31.

A clinical S. aureus strain derived from patient skin was then added onto RHEs at day 12 for 24 hours. Control microbiotic RHEs were also performed without inflammatory challenge. Epidermal alterations were then analyzed by histology and immunostaining, transmission electron microscopy and western blotting. IL-8 quantification was performed using AlphaLISA immunoassay kit.

Results

Treated RHEs exhibited the reported AD-associated alterations: spongiosis and dysregulated expression of epidermal differentiation proteins (filaggrin, loricrin, claudin-1 and corneodesmosin). Moreover, we particularly evidenced an abnormal lamellar body distribution and an impaired synthesis of Rab11a GTPase, a key regulator of lamellar body biogenesis and trafficking.

The model was also characterized by a high keratinocyte-release of the inflammatory cytokine IL-8. Interestingly, we showed that S. aureus adhered and grew better in presence of the inflammatory cocktail than without.

Conclusion

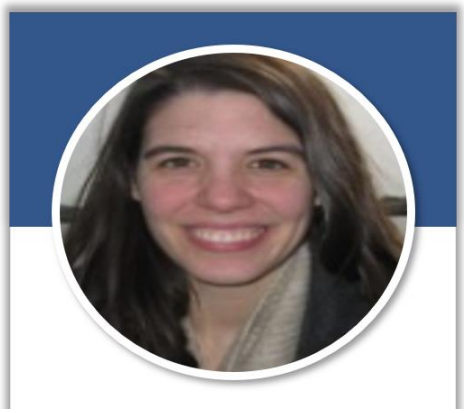
Our inflammatory RHE model including S. aureus well mimics the impairments observed in AD, at the physical and immune levels, and recapitulates some of the vicious loops involved in the AD pathophysiology where microbial imbalance occurs. Moreover, our results strongly suggest that S. aureus acquires higher virulence potential when the epidermis is challenged with inflammatory cytokines, thus later contributing to the chronic inflammatory status. Our new inflammatory and microbiotic AD model may be considered for in vitro screening of cosmetics or therapeutic compounds to open the way to new global preventive and therapeutic strategies for AD.

Why is this important to the industry?

AD is a chronic, inflammatory skin disease which results in widespread rashes and patches of itchy skin.

The prevalence rate of AD is rising worldwide, and AD affects 15-20% of children and 3-10% of adults.

While there are many medical and non-medical treatments, they are not all effective and many people have troubling controlling their AD. Developing more accurate models to select new performing and easy to use ingredients is important for the skin care market.



Innovative Scientist with 10 years of experience leading and collaborating with cross-functional teams in R&D, project management, product development, and method development within the biotechnology sector.