

- 6 Chadwick X, Loescher LJ, Janda M, Soyer HP. Mobile medical applications for melanoma risk assessment: false assurance or valuable tool? 2014 47th Hawaii Int Conf Syst Sci 2014; 2675–84.
- 7 Wolf JA, Moreau JF, Akilov O et al. Diagnostic inaccuracy of smartphone applications for melanoma detection. *JAMA Dermatol* 2013; **149**:422–6.
- 8 Kassianos AP, Emery JD, Murchie P, Walter FM. Smartphone applications for melanoma detection by community, patient and generalist clinician users: a review. *Br J Dermatol* 2015; **172**:1507–18.
- 9 International Society for Digital Imaging of the Skin. ISIC: melanoma project. 2014. Available at <http://isdis.net/index.php/projects> (last accessed 5 March 2015).

## Deficiency in barrier function and slow barrier recovery in atopic dermatitis does not depend only on the *FLG* mutation status

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### ORIGINAL ARTICLE, p 1519

The epidermal barrier is a complex and dynamic structure that senses and responds to external stresses to maintain skin and body homeostasis. External aggressions cause barrier disruption immediately followed by barrier repair with keratinocyte proliferation/differentiation, extracellular lipid extrusion and cytokine release, which can influence both barrier repair and the type of local and systemic immune response to exogenous stresses.

Filaggrin is important for skin barrier function, namely in the differentiation of keratinocytes to form the stratum corneum (SC, binding of intracellular filaments with the cornified envelop as the scaffold for the intercellular lamellar lipid bilayers), for SC hydration (formation of natural moisturizing factor from filaggrin degradation), for ultraviolet radiation (UVR) protection (histidine from filaggrin is converted to the UVR-absorbing trans-urocanic acid) and for lowering skin pH which prevents microbial colonization and interleukin (IL)-1 $\alpha$  and IL-1 $\beta$  release.<sup>1</sup>

Filaggrin is highly deficient in most cases of atopic dermatitis (AD), either due to genetic *FLG* mutations, epigenetic modification or secondary to the local effect of T-helper (Th) 2 cytokines.<sup>1</sup> But barrier defect in AD is much more than filaggrin deficiency. Within the barrier a reduced amount and modified quality of ceramides affect lipid bilayers, a disequilibrium in the protease/antiprotease system affects SC cohesion, an increased pH allows *Staphylococcus aureus* colonization and cytokine release, a reduced expression of tight-junction proteins (claudin-1) increases subcorneal permeability to large molecules and allows permeation of Langerhans cell dendrites into the SC.<sup>2,3</sup> This barrier deficiency is responsible for increased transepidermal water loss with dry skin, favours sensitization to environmental allergens and increases susceptibil-

ity to chemical irritants present in many of our daily hygiene products, such as the surfactant sodium lauryl sulfate (SLS).<sup>4</sup>

Moreover, as shown by Bandier et al.,<sup>4</sup> independent of the *FLG* mutation status in AD, after an acute SLS aggression, barrier recovery is much slower. Therefore, there is a higher chance for another exposure to an irritant before complete barrier recovery with further long-lasting barrier disruption with all its consequences.

In fact, there seems to be a link between epidermal barrier disruption in AD and a Th2 skewed immune response, pruritus mediated by IL-31,<sup>5</sup> predominance of type 2 innate lymphoid cells in AD skin<sup>1</sup> and, eventually, with sequential development of food allergy, asthma and rhinitis, which characterize the 'atopic march'. Thymic stromal lymphopoietin (TSLP), elevated in the skin and serum of patients with AD, is an important candidate to link the disrupted barrier with immunological abnormalities, as it is highly involved in Th2 sensitization and has been shown to favour development of asthma and the 'atopic march' in animal models.<sup>2,6</sup>

Pharmacological treatment (corticosteroids and calcineurin inhibitors) improves disrupted skin barrier in AD, but additional daily measures that prevent further barrier disruption (skin cleansing with tepid water and mild surfactants) or that enhance barrier recovery (regular use of emollients) should also be recommended. Moreover, as emollients were also shown to reduce skin production of TSLP<sup>7</sup> and other pro-inflammatory cytokines, they may also contribute to halt the 'atopic march'. Nevertheless, studies are needed to confirm if these and other intervention measures in AD prevent the 'atopic march' in humans.<sup>8</sup>

## Conflicts of interest

None declared.

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## References

- 1 Thyssen JP, Kezic S. Causes of epidermal filaggrin reduction and their role in the pathogenesis of atopic dermatitis. *J Allergy Clin Immunol* 2014; **134**:792–9.
- 2 De Benedetto A, Kubo A, Beck L. Skin barrier disruption: a requirement for allergen sensitization? *J Invest Dermatol* 2012; **132**:949–63.
- 3 Batista DI, Perez L, Orfali RL et al. Profile of skin barrier proteins (filaggrin, claudins 1 and 4) and Th1/Th2/Th17 cytokines in adults with atopic dermatitis. *J Eur Acad Dermatol Venerol* 2014; doi: 10.1111/jdv.12753 [Epub ahead of print].
- 4 Bandier J, Carlsen BC, Rasmussen MA et al. Skin reaction and regeneration after single sodium lauryl sulfate exposure stratified by filaggrin genotype and atopic dermatitis phenotype. *Br J Dermatol* 2015; **172**:1519–29.

- 5 Melnik BC. The potential role of impaired Notch signalling in atopic dermatitis. *Acta Derm Venereol* 2015; **95**:5–11.
- 6 Leyva-Castillo JM, Hener P, Jiang H, Li M. TSLP produced by keratinocytes promotes allergen sensitization through skin and thereby triggers atopic march in mice. *J Invest Dermatol* 2013; **133**:154–63.
- 7 Sano Y, Masuda K, Tamagawa-Mineoka R et al. Thymic stromal lymphopoietin expression is increased in the horny layer of patients with atopic dermatitis. *Clin Exp Immunol* 2013; **171**:330–7.
- 8 Bieber T, Cork M, Reitamo S. Atopic dermatitis: a candidate for disease-modifying strategy. *Allergy* 2012; **67**:969–75.

## Automated Melasma Area and Severity Index scoring

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### ORIGINAL ARTICLE, p 1535

Melasma is a common pigmentary disorder mainly affecting women with skin phototype III–V.<sup>1</sup> There is an effort to create standardized tools for the measurement of melasma treatment outcome. The Melasma Area and Severity Index (MASI), developed by Kimbrough-Green et al. in 1994<sup>2</sup> is the most frequently used measure. The MASI calculations are based on subjective assessments of three factors: area of involvement (A), darkness (D) and homogeneity (H), on four regions of the face: forehead (f), right malar (rm), left malar (lm) and chin (c), corresponding to 30%, 30%, 30% and 10% of the facial area, respectively. The area of melasma in each of the four regions is graded from 0 to 6 (0, no involvement; 1, < 10%; 2, 10–29%; 3, 30–49%; 4, 50–69%; 5, 70–89%; 6, 90–100%). Darkness and homogeneity are assessed on a scale from 0 to 4 (0, absent; 1, slight; 2, mild; 3, marked; 4, maximum). Pandya et al.<sup>3</sup> proposed a modified MASI (mMASI), which excluded homogeneity as a scoring factor, and was assessed to be reliable as a MASI score.<sup>3</sup> To date, MASI and mMASI are the most widely used validated instruments and have been used universally in melasma clinical trials. The mMASI score is calculated as follows with total score ranging from 0 to 24:

$$\text{mMASI} = 0.3A(f)D(f) + 0.3A(\text{rm})D(\text{rm}) + 0.3A(\text{lm})D(\text{lm}) + 0.1A(c)D(c)$$

In this issue of the *BJD*, Tay et al.<sup>4</sup> generated an automated MASI (aMASI) using digital image analysis, by feeding semi-automatically calculated area of involvement and level of darkness into the mMASI formula. Three facial photographs are required, one frontal picture including forehead and chin, one from the left side and one from the right for malar areas. To obtain an aMASI score, the normal skin area was selected manually to be a reference point. After excluding nonskin areas, thresholding was performed to determine the extent of

the lesion. The average darkness of pixels in melasma was calculated using the difference in the Lab values<sup>5</sup> of normal and affected skin. These are values that are often used to assess colorimetry-based measurements. Baseline and post-treatment aMASI scores were validated in 29 patients with melasma and showed good correlation with clinically assigned mMASI scores.<sup>4</sup>

The aMASI, considered to be an objective assessment technique, can reduce interrater variability. Unlike with mMASI, the melasma area involvement score in aMASI is not banded, which reveals actual and more reliable changes in scores. This is reflected in the lower associated standard deviation of the aMASI scores compared with mMASI scores, as presented by Tay et al.<sup>4</sup> in their Table 1.<sup>4</sup> When using aMASI, concurrent treatment in patients with melasma and concomitant pigmentary conditions can affect a clinical interpretation. The automated methods specifically identifying melasma from other pigmentation should be developed further. Besides, aMASI potentially can be modified to utilize it in other hyperpigmentation, hypopigmentation and depigmentation disorders.

The authors have shown their intent to make the aMASI algorithm downloadable in the near future. This will certainly make the scoring standardized and provide time efficiency. However, a comprehensive evaluation with validation of aMASI across a larger and diverse skin colour population needs to be done before this goal can be accomplished.

## Conflicts of interest

None declared.

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## References

- 1 Sheth VM, Pandya AG. Melasma: a comprehensive update: part I. *J Am Acad Dermatol* 2011; **65**:689–97.
- 2 Kimbrough-Green CK, Griffiths CE, Finkel LJ et al. Topical retinoic acid (tretinoin) for melasma in black patients. A vehicle-controlled clinical trial. *Arch Dermatol* 1994; **130**:727–33.
- 3 Pandya AG, Hynan LS, Bhore R et al. Reliability assessment and validation of the Melasma Area and Severity Index (MASI) and a new modified MASI scoring method. *J Am Acad Dermatol* 2011; **64**:78–83, e1–2.
- 4 Tay EY, Gan EY, Tan VWD et al. Pilot study of an automated method to determine Melasma Area and Severity Index. *Br J Dermatol* 2015; **172**:1535–40.
- 5 Khan R, Hanbury A, Stöttinger J et al. Color based skin classification. *Pattern Recogn Lett* 2012; **33**:157–63.