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Brown, S. J.

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JEADV Commentary

Increased filaggrin expression in oral lichenoid lesions: is this cause or effect?

Sara J Brown

Professor of Molecular & Genetic Dermatology, *Wellcome Trust Senior Research Fellow in Clinical Science, Honorary Consultant Dermatologist*

Skin Research Group,
School of Medicine,
Ninewells Hospital & Medical School,
Jacqui Wood Centre level 7,
James Arrott Drive,
University of Dundee,
Dundee DD1 9SY

T +44 (0) 1382 383210
E s.j.brown@dundee.ac.uk

Filaggrin is expressed in the outermost layers of the human epidermis;[1] it plays a central role in skin barrier formation through its multiple functions from the pro-protein which has calcium-binding domains, to the filaggrin monomers which aggregate keratin filaments, and to its constituent amino acids which are released in the stratum corneum contributing to water retention, ultraviolet B absorption and acidification.[2] Loss of function mutations in the gene encoding filaggrin (*FLG*) cause ichthyosis vulgaris[3] and strongly predispose to eczema as a manifestation of skin barrier dysfunction.[4] Whilst *FLG* null mutations lead to a marked reduction in filaggrin in skin, factors that increase the thickness of the stratum corneum may be considered to increase filaggrin expression in a specific or a non-specific way. Whilst filaggrin is intimately associated with cornification, it is interesting to note that *FLG* is still expressed in the non-keratinised areas of buccal mucosa.[5]

Lichen planus (LP) is an inflammatory disease of unknown aetiology. The increased expression of keratins 1, 2, 10 and 11, along with a reduction in expression of keratins 4 and 13 have been reported in buccal mucosal LP.[6] It has been proposed that barrier impairment may be a preceding event in the pathogenesis of LP, or it may occur as a secondary effect resulting from disturbance in keratinocyte differentiation.[7] Opposing hypotheses can therefore be proposed: that filaggrin expression is either increased or decreased within the lesional epidermis in LP.

The study by Larsen *et al.* reported in this edition of the *JEADV*[8] set out to test several hypotheses relating to the relationship between oral lichenoid lesions (OLL, including oral LP), filaggrin expression, *FLG* mutations and co-associated skin conditions. 38 patients with OLL (including 19 with oral LP) and 11 with non-specific stomatitis were compared with 29 unaffected controls. Immunoflourescent staining of buccal mucosal biopsy specimens showed a marked increase in filaggrin expression in 21% of patients with OLL but none of the healthy controls; conversely there was a marked reduction in filaggrin immunostaining observed in 15% of healthy controls compared with 6% of patients with OLL. The differences in filaggrin staining showed no association with the presence or absence of loss of function mutations in *FLG.* The patients with OLL also did not have an increased prevalence of dermatological disorders (other than LP) when compared with controls.

These findings must be interpreted with caution because of the small sample size. However, the observation of an increase in filaggrin expression in OLL that is independent of *FLG* genotype and unrelated to other skin disorders implies that the increased filaggrin expression is a secondary effect of local inflammation and hyperkeratosis rather than a primary aetiological factor. Filaggrin binds to keratins 2 and 10 and may therefore be increased in consort with them.[6] The absence of association of LP with filaggrin down-regulation sheds doubt on the hypothesis that skin barrier dysfunction contributes to the primary pathogenesis of lichenoid inflammation; the underlying aetiology of oral LP continues to be enigmatic.

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